ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY

FOUNDED IN 1892

VOLUME 68

Editor

ARTHUR W. PROETZ, M.D.
12 Westmoreland Place, St. Louis 8

Associate Editor

BEN H. SENTURIA, M.D.
500 N. Skinker Boulevard, St. Louis 5

Editorial Board

VICTOR R. ALFARO, M.D. *Washington, D.C.*
LAWRENCE R. BOIES, M.D. . *Minneapolis*
LOUIS H. CLERF, M.D. . *St. Petersburg, Fla.*
FRED W. DIXON, M.D. . . . *Cleveland*
EDMUND J. FOWLER, JR., M.D. *New York*
DAVID R. HIGBEE, M.D. . *San Diego, Calif.*
ANDERSON C. HILDING, M.D. . . *Duluth*
FREDERICK T. HILL, M.D. . *Waterville, Me.*
JAMES H. MAXWELL, M.D. *Ann Arbor, Mich.*
BERNARD J. MCMAHON, M.D. . *St. Louis*
LEROY A. SCHALL, M.D. . . . . *Boston*
FRANCIS A. SOOY, M.D. . . *San Francisco*
JUERGEN TONNDORF, M.D. . *Iowa City, Ia.*
O. E. VAN ALYEA, M.D. . . . *Chicago*

Published Quarterly

BY THE

ANNALS PUBLISHING COMPANY

Business Office • P. O. Box 1345, Central Station 88

ST. LOUIS, MO., U.S.A.

COPYRIGHT, 1960
ANNALS PUBLISHING COMPANY

Annual Subscription in United States, $14.00 in Advance.
Canada, $14.40. Other Countries, $14.80.

Table of Contents, Volume 68

MARCH, 1959—NUMBER 1

PAGE

I—Stimulation Deafness, Cochlear Patterns, and Significance of Electrical Recording Methods. Merle Lawrence, Ph.D., David Wolsk, M.A., Robert D. Burton, M.D., Ann Arbor, Michigan 5

II—Possibilities for Therapy with Enzymes. Sol Sherry, M.D., St. Louis, Mo. 34

III—Epidermoid Cholesteatoma and Cholesterol Granuloma. Experimental and Human. I. Friedmann, London, England 57

IV—Treatment of Sinus Barotrauma. Ralph N. Kraus, Colonel, USAF (MC), Randolph Air Force Base, Texas 80

V—Hearing Problems Associated with Cleft Palate. Maurice H. Miller, Ph.D., Brooklyn, N.Y. 90

VI—Laryngocele and Laryngeal Cancer. L. Pietrantoni, D. Felisati and A. Finzi, Milan, Italy 100

VII—The Use of the Scanograph in the Diagnosis of Masses at the Base of the Tongue. James A. Harrill, M.D., Joseph E. Whitley, M.D., I. Meschan, M.D., Winston-Salem, N. C. 108

VIII—The Too Small Mouth in Patients with "Plummer-Vinson" Syndrome. R. J. H. Kruisinga and Eelco Huizinga, Groningen, Netherlands 115

IX—Chemical Burns of the Mouth, Pharynx and Esophagus. Bobby R. Alford, M.D., Herbert H. Harris, M.D., Houston, Texas 122

X—Electronystagmographic Studies of Vestibular Function. Method and Procedure. Godfrey E. Arnold, M.D., Vito Giuliani, M.D., and George Stephens, M.D., New York, N. Y. 129

XI—Electrophysiological Studies of the Labyrinth of the Guinea Pig. I. The DC Resting Potentials of the Semicircular Canals. II. The Changes of the DC Potentials Inside the Ampullae of the Semicircular Canals During Experimental Cupula Deviations. D. Trincker, M.D. III. The AC Potentials (Microphonics) from the Vestibular Apparatus. D. Trincker, M.D. and C. J. Partsch, M.D., Erlangen, Germany 145

XII—Teratoma of the Floor of the Mouth. Report of a Case. Charles R. Smathers, M.D., New York, N. Y. 159

XIII—The Effect of Cutting the Labyrinthine Artery on the Oxygen Tension in the Labyrinth. Yasushi Koide, Ph.D., M.D., Makoto Yoshida, M.D. and Masaru Konno, M.D., Niigata, Japan 164

PAGE

XIV—Rubella in Pregnancy. Fetal Pathology in the Internal Ear. J. E. Gray, Newcastle-upon-Tyne, Eng. 170

XV—Secretory Sialography in Diseases External to the Major Salivary Glands. Irving M. Blatt, M.D., John E. Magielski, M.D., James H. Maxwell, M.D. and John F. Holt, M.D., Ann Arbor, Mich. 175

XVI—Chronic Complete Traumatic Occlusion in the Larynx Secondary Endotracheal Anesthesia and Its Plastic Correction. Donald F. Proctor, M.D. and Milton T. Edgerton, M.D., Baltimore, Md. 187

XVII—Auditory Sensitivity and the Magnitude of the Cochlear Potential. Thomas E. McGill, Ph.D., Williamstown, Mass. 193

XVIII—Facial Kinetograph. A Description of a Method for the Study of New Treatments for Facial Paralysis. August L. Stemmer, M.D., Boston, Mass. 208

XIX—Lymphosarcoma: A Problem for the Nose and Throat Specialist. Albert P. Seltzer, M.D., Philadelphia, Pa. 222

XX—An Analysis of One Thousand Cases of Hearing Loss in Children. Frank Kodman Jr., Ph.D., Gerald Sperrazzo, M.A., Lexington, Ky. 227

Abstracts of Current Articles 234

Books Received 261

Notices 262

Officers of the National and International Otolaryngological Societies 270

JUNE, 1959—NUMBER 2

XXI—Electron Microscopic Observations on a Glomus Jugulare Tumor. J. D. Boyd, J. D. Lever and A. N. Griffith, Cambridge, Eng. 273

XXII—Electronystagmographic Studies of Vestibular Function. II. Basic Problems of Calibration. Godfrey E. Arnold, M.D. and Francis Miskolczy-Fodor, M.D., New York, N. Y. 284

XXIII—Otitic Meningitis in the Antibiotic Era: Observations on 28 Adult Patients Treated in the Los Angeles County Hospital, 1950-1957. H. James Hara, M.D., Los Angeles, Calif. 305

XXIV—Primary Quinsy Tonsillectomy. G. H. Bateman, M.A., B.M., J. Kodicek, M.B., London, Eng. 315

XXV—The Effects of Cations on Labyrinthine Activity. Yasushi Koide, Ph.D., M.D., Kokichi Seki, M.D. and Masanori Morimoto, M.D., Niigata-Shi, Japan 322

Scientific Papers of the American Laryngological Association

XXVI—Osteomyelitis of the Frontal Bone. Harry P. Schenck, M.D., Philadelphia, Pa. 336

PAGE

XXVII—An Extralaryngeal Approach for Certain Benign Lesions of the Larynx. LeRoy A. Schall, M.D., Boston, Mass. 346

XXVIII—Carcinoma of the Nasopharynx. An Analysis of Thirty-four Cases and a Preliminary Report on Palatal Fenestration in Its Management. L. Q. Pang, M.D. (by invitation), Honolulu, Hawaii 356

XXIX—The Simulated Larynx. C. J. Campbell, M.D. (by invitation) and John A. Murtagh, M.D., Hanover, N. H. 372

XXX—Surgery of the Neck Following Radiation Therapy for Cancer. Walter P. Work, M.D., San Francisco, Calif. 393

XXXI—The Diagnosis of Chronic Inflammatory Lesions of the Sphenoid Sinus. J. H. Maxwell, M.D., B. Jay Hill, M.D. (by invitation), Ann Arbor, Mich. 411

XXXII—Concerning the Criteria of Operability in Laryngeal Cancer. John J. O'Keefe, M.D., Philadelphia, Pa. 453

XXXIII—Anatomical Observations Concerning the Laryngeal Appendix. Edwin N. Broyles, M.D., Baltimore, Md. 461

XXXIV—Pseudosarcoma of the Pharynx and Larynx. Daniel C. Baker, Jr., M.D., New York, N. Y. 471

XXXV—Cystic Fibrosis of the Pancreas and Nasal Mucosa. Moses H. Lurie, M.D. (by invitation), Boston, Mass. 478

XXXVI—Causes of Failure in Surgical Treatment of Malignant Tumors of the Larynx. Charles M. Norris, M.D., Philadelphia, Pa. 487

XXXVII—Histochemical Studies of the Pathogenesis of Nasal Polyps. Alex Weisskopf, M.D. and Helen F. Burn, M.S. (by invitation), San Francisco, Calif. 509

XXXVIII—Wegener's Granulomatosis. Joseph P. Atkins, M.D. and Sylvan H. Eisman, M.D. (by invitation), Philadelphia, Pa. 524

Scientific Papers of the American Broncho-Esophagological Association

XXXIX—Broncholithiasis. Herman J. Moersch, M.D., Herbert W. Schmidt, M.D., Rochester, Minn. 548

XL—Interesting Foreign Bodies of the Food and Air Passages. A Small Series of Cases Reflecting Difficulty in Management or Unusual Clinical Features. V. K. Hart, M.D., Charlotte, N. C. 564

XLI—Experiences with Dilatation of the Esophagus Following Surgery for Esophageal Atresia. Lewis E. Morrison, M.D., Indianapolis, Ind. 580

XLII—Should Patients Be Hospitalized for Peroral Endoscopic Procedures? Chevalier L. Jackson, M.D., Philadelphia, Pa. 596

Abstracts of Current Articles 598

Books Received 606

Notices 607

Officers of the National and International Otolaryngological Societies 611

SEPTEMBER, 1959—NUMBER 3

PAGE

XLIII—Traumatic Stricture of the Larynx. L. Reed Cranmer, M.D., Toledo, Ohio 613

XLIV—Temporal and Pitch Aspects of Superior Esophageal Speech. John C. Snidecor, Ph.D., Goleta, Calif., and E. Thayer Curry, Ph.D., Urbana, Ill. 623

XLV—Notes on the Mucosa of the True Vocal Cord. J. B. Gregg, M.D., Sioux Falls, S. D. 637

XLVI—Electronystagmographic Studies of Vestibular Function: III. The Influence of Various Electrode Arrangements. Francis Miskolczy-Fodor, M.D., and Godfrey E. Arnold, M.D., New York, N. Y. 652

Scientific Papers of the American Otological Society

XLVII—An Interpretation of the Mechanical Detector Action of the Cochlea. Hallowell Davis with Donald H. Eldredge (by invitation), St. Louis, Mo. .. 665

XLVIII—Sampling Auditory Responses at the Cortical Level. A Routine for EER-Audiometric Testing. A. J. Derbyshire, Ph.D., Detroit, Mich., and J. C. Farley, Ph.D. (by invitation), Chicago, Ill. 675

XLIX—The Ototoxicity of Kanamycin. Joseph E. Hawkins, Jr., Ph.D. (by invitation), New York, N. Y. 698

L—Fluid Ears and Nerve Deafness Circa 1835. Gordon D. Hoople, M.D., Wesley H. Bradley, M.D. (by invitation), Syracuse, N. Y. 716

LI—Acoustic Trauma Following Intermittent Exposure to Tones. Donald H. Eldredge, M.D. (by invitation), Walter P. Covell, M.D., Ph.D. (by invitation), and R. Patrick Gannon, M.B., Ch.B. (by invitation), St. Louis, Mo. 723

LII—An Experimental Study of the Dynamic Circulation of the Labyrinthine Fluids. Geza Jako, M.D. (by invitation), Francis L. Weille, M.D., Patricia E. Palmer, A.B. (by invitation), John W. Irwin, M.D. (by invitation), Boston, Mass. 733

LIII—Long Term Results of Surgery for Otosclerotic Deafness. Theodore E. Walsh, M.D., St. Louis, Mo. 740

LIV—The Treatment of Ménière's Disease with Ultrasonic Waves. Further Observations. Franz Altmann, M.D., and Jules G. Waltner, M.D. (by invitation), New York, N. Y. 750

LV—Presbyacusis. The Aging Ear. Edmund Prince Fowler, M.D., New York 764

LVI—Nihil Sub Sole Novum. Lyle M. Sellers, M.D., Dallas, Texas 777

LVII—Aural Embryopathies. George Kelemen, M.D., Boston, Mass. 798

LVIII—Cochlear Blood Flow During Hypothermia. H. B. Perlman, M.D., Robert Kimura, A.B. (by invitation) and Robert A. Butler, Ph.D. (by invitation), Chicago, Ill. 803

PAGE

LIX—Experimental Observations on Postural Nystagmus in the Cat. César Fernandez, M.D. (by invitation), Rene Alzate, M.D. (by invitation) and John R. Lindsay, M.D., Chicago, Ill. 816

LX—Sudden Deafness and Bell's Palsy: A Common Cause. William H. Saunders, M.D. (by invitation) and William H. Lippy, M.D. (by invitation), Columbus, Ohio 830

LXI—Certain Problems in Tympanoplasty. Fred R. Guilford, M.D., Houston, Texas 838

LXII—The Surgical Treatment of Facial Paralysis and Traumatic Conductive Deafness in Fractures of the Temporal Bone. Hollie E. McHugh, M.D., Montreal, Canada 855

Scientific Papers of the American Broncho-Esophagological Association

LXIII—Perforation of the Esophagus After Use of a Digestant Agent. Report of Case and Experimental Study. Howard A. Andersen, M.D., Philip E. Bernatz, M.D. (by invitation), John H. Grindlay, M.D. (by invitation), Rochester, Minn. 890

LXIV—Pulmonary Function Tests as an Adjunct in Bronchology. James J. O'Neil, M.D., Omaha, Nebr. 897

LXV—The Management of Esophageal Varices in Children by Injection of Sclerosing Agents. Blair Fearon, M.D., and Andrew Sass-Kortsak, M.D. (by invitation), Toronto, Canada 906

Abstracts of Current Articles 916

Notices 929

Officers of the National and International Otolaryngological Societies 931

DECEMBER, 1959—NUMBER 4

PAGE

LXVI—Otorhinolaryngologic Problems in the Mother and the Newborn Infant. Francis L. Lederer, M.D., Chicago, Ill. 933

LXVII—Ultrastructure of the Tracheal Ciliated Mucosa in Rat and Man. J. Rhodin, M.D., New York, N. Y. 964

LXVIII—The Cochlear Potentials and Their Relation to Hearing. Ernest Glen Wever, Ph.D., Princeton, N. J. 975

LXIX—Vocal Rehabilitation by Autogenous Vein Graft. John J. Conley, M.D., New York N. Y. 990

LXX—Experiences with the Fenestra Ovalis Technique of Shea. A Preliminary Clinical and Experimental Report. David Myers, M.D., S. D. Erulkar, D.Phil., Woodrow D. Schlosser, M.D., Lindsay Pratt, M.D., Richard A. Winchester, Ph.D., Philadelphia, Pa. 996

LXXI—Middle Ear Effusions Produced Experimentally in Dogs. I. Microscopic and Bacteriologic Findings. Jacob Sade, M.D., Charles D. Carr, M.T., Ben H. Senturia, M.D., St. Louis, Mo. 1017

LXXII—Middle Ear Effusions Produced Experimentally in Dogs. II. Some Biochemical and Electrophoretic Properties. Carl F. Gessert, Ph.D., E. S. Baumann, B.A., Ben H. Senturia, M.D., St. Louis, Mo. 1028

LXXIII—The Effects of Topical Anesthetics upon the Ear. W. E. Rahm, Jr., W. F. Strother, W. L. Gulick, J. F. Crump, Princeton, N. J. 1037

LXXIV—The Endoscopic Management of Congenital Atresia of the Esophagus with or without Tracheo-esophageal Fistula and of Congenital Tracheo-esophageal Fistula without Atresia of the Esophagus. Blair Fearon, M.D., Toronto, Canada 1047

LXXV—Experimental Fracture of the Stapes in Cats. George T. Singleton, M.D. and Harold F. Schuknecht, M.D., Detroit, Mich. 1069

LXXVI—The Lateral Pharyngeal Cleft. George R. L. Gaughran, Ph.D., Ann Arbor, Michigan 1082

LXXVII—Adenoid Cystic Epithelioma. "Brooke-Fordyce Disease." Fatma H. Abdin, M.D. and Abdel Salam El-Barbari, F.R.C.S., Cairo, Egypt 1097

LXXVIII—Sarcoma of the Head and Neck in Childhood. H. Markowicz, M.D. and E. Shanon, M.D., Tel Aviv, Israel 1105

LXXIX—Middle Ear Muscle Activity at Moderate Sound Levels. F. Blair Simmons, M.D., Stanford, Calif. 1126

LXXX—Chondroma of the Larynx. Report of a Case and a Review of the Literature. William L. Walter, M.D., Staten Island, N. Y. 1144

LXXXI—Headaches Caused by Bruxism. Woodrow S. Monica, D.M.D., Orange, N. J. 1159

LXXXII—Study of Some Features of the Neuro-epithelia of the Internal Ear in the Chicken. Consuelo Savin V., M.S., Mexico DF, Mexico 1163

LXXXIII—Deafness Following Short-Term Exposure to Industrial Noise. S. L. Shapiro, M.D., Chicago, Ill. 1170

LXXXIV—Bilateral Temporomandibular Intra-articular Ankylosis Following Rheumatic Fever. Report of a Case. Alvin C. Poweleit, M.D., Covington, Ky., and Robert C. Kratz, M.D., Newport, Ky. 1182

LXXXV—Two New Methods for the Assessment of Central Auditory Functions in Cases of Brain Disease. Joseph Matzker, M.D., Mainz, Germany 1185

LXXXVI—Chordoma. Study of a Retropharyngeal Case. Jacques Turcot, M.D., J. P. Després, M.D. and Marc Beaudet, M.D., Québec, Canada 1198

PAGE

LXXXVII—Reconstruction of the Laryngeal Lumen in Chronic Laryngeal Stenosis. Charles R. Smathers, M.D., Jacksonville, Fla. 1205

Abstracts of Current Articles 1213

Books Received 1225

Notices 1227

Officers of the National and International Otolaryngological Societies 1232

Index of Authors 1234

Index of Titles 1236

ANNALS
OF
OTOLOGY, RHINOLOGY
AND
LARYNGOLOGY

VOL. 68 MARCH, 1959 No. 1

I

STIMULATION DEAFNESS, COCHLEAR PATTERNS, AND SIGNIFICANCE OF ELECTRICAL RECORDING METHODS

MERLE LAWRENCE, PH.D.
DAVID WOLSK, M.A.
ROBERT D. BURTON, M.D.
ANN ARBOR, MICHIGAN

The organ of Corti, extending as a continuous structure from base to apex along the basilar membrane, vibrates in accordance with certain patterns, and the sensory cells, distorted because of the movement, give rise to an alternating-current potential the frequency of which corresponds to that of the driving vibration. This potential is believed to be responsible for the initiation of the nerve impulses that carry the information to the higher centers of the brain.

The all-important structures in the inner ear are the sensory cells. All of the other inner-ear structures are there for one of two purposes: to provide a means for conveying the vibrations to the sensory cells or to furnish the proper environment for their metabolic processes and survival. Any interference with the normal activity of these supporting structures changes the capabilities of the sensory cells and causes an inner-ear or cochlear deafness. The direct result of condi-

From the Physiological Acoustics Laboratory, Department of Otolaryngology and Institute of Industrial Health, School of Medicine, University of Michigan. This investigation was supported in part by the Research and Development Division, Office of the Surgeon General, Department of the Army, Under Contract No. DA-49-007-MD-634 and by funds for research in Human Resources, University of Michigan.

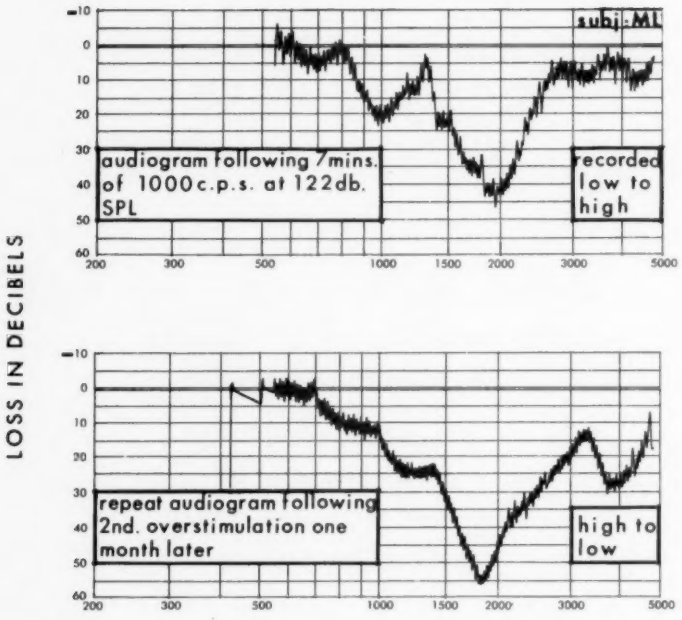


Fig. 1.—Sweep-frequency audiograms following the indicated overstimulation. The lower audiogram was made to check the possibility that the sharp frequency notch an octave above the overstimulating frequency was not the result of fatigue for the higher frequencies as the low frequencies were being swept through.

tions that affect the sensory cells is a decrease in the magnitude of the alternating-current potential, and the final effect is a hearing loss as determined by an audiogram.

In animal studies of inner-ear deafness, recording the cochlear potentials is the best method available for determining functional changes in the organ of Corti, and, to date, the type of inner-ear lesion studied most thoroughly by this method has been produced by overstimulation. From this work, however, a disturbing observation has arisen: *the audiometric measures of hearing loss for various frequencies do not conform with the electrical measures.* Resolution of this problem is important for it may throw light on the locus of frequency-analysis properties of the ear, but, for the moment, the nature of the discrepancy is sufficiently abstruse to necessitate an examination of the conditions under which it arises.

Whenever the human ear is stimulated by sound there is an immediate shift in sensitivity which can be measured by appropriate audiometric means. Whether it is temporary or permanent this characteristic elevation of the threshold represents a hearing loss, and because a hearing loss is a sign of malfunction somewhere in the auditory system it is quite important, from a clinical standpoint, that the locus of the abnormal condition be determined.

Roughly, we can divide the auditory system into two areas where the changes responsible for the audiometric shift might occur: the organ of Corti and the acoustic-nerve pathways. Audiometric measures, of course, represent the response of the entire auditory system while the results of the technique of recording the cochlear potentials represent the activity of all structures up to the point of generation of these potentials, which includes the sensory cells of the organ of Corti. Theoretically, a comparison of results from the two methods should help pinpoint the locus of abnormality.

Figure 1 presents audiograms made with a sweep-frequency audiometer of a subject's hearing immediately following the presentation of a 1000 cps tone at 122 db above .0002 dyne per sq cm for 7 minutes. In the upper audiogram the frequency was swept from low to high. To obviate the possibility that the lower frequencies had fatigued the ear to higher frequencies, the subject's ear was again stimulated with the same frequency and intensity one month later after full recovery had taken place, and a high-to-low sweep-frequency audiogram taken immediately afterwards. This is shown in the lower audiogram. With slight variation the same pattern shows up in both; the maximum threshold shift has not occurred at the frequency of stimulation but approximately one octave higher. This observation has been made before and does not really concern us here, but the fact that the shift is sharply notched is of interest.

Figure 2 shows an electrical audiogram recorded from a guinea pig after the identical degree of stimulation: 7 minutes of 1000 cps at 122 db above .0002 dyne per sq cm. In this instance there is a generalized loss, greater for the middle frequencies than for the extreme lows and highs. Similar results have been shown before.[1] No specific frequency shift as shows up in the audiometric examination of the human ear appears in this organ-of-Corti response. There are only two points of general similarity: the center frequencies suffer a greater loss than do the extreme lows and highs and the higher frequencies are hurt more than the lows.

There are two possible explanations for the differences between Figures 1 and 2: the technique of recording the potentials may have

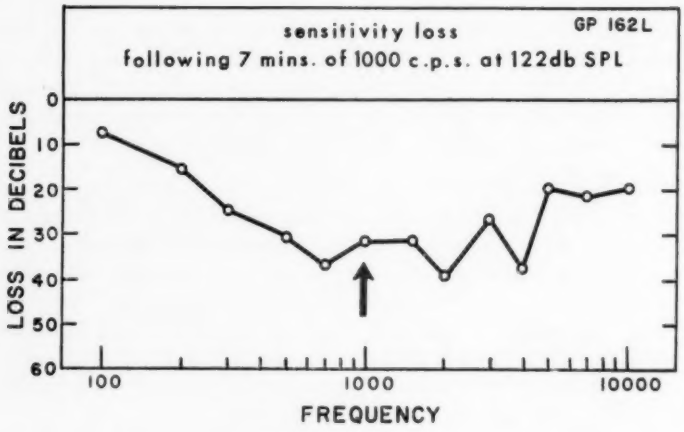


Fig. 2.—Electrical audiogram made by recording the cochlear potentials with a platinum-foil electrode on the round window and an indifferent electrode in the temporalis muscle. The curve shows the loss at various frequencies following overstimulation at a frequency (arrow) and intensity identical to that of Figure 1.

characteristics that prevent the specific loss at some particular region of the organ of Corti from being recorded, or the picture of general loss could be more or less accurate indicating that sharp frequency loss seen audiometrically is the result of neural "interpretation" of what has happened along the basilar membrane.

The recording of Figure 2 was made by means of a platinum-foil electrode on the round-window membrane and an indifferent electrode in the temporalis muscle. Appropriate associated electronic equipment was used to filter out the nerve action potentials.

Both Davis[2] and Tasaki[3] have maintained that such an electrode placement records from only the basal half of the basal turn of the cochlea and therefore, necessarily, shows a picture of generalized loss because the specific region of maximum damage is not in this basal region. They hold that the only way to examine the functional changes in the region of maximum loss is by placing in the supposed vicinity of this damage a pair of "differential" electrodes,[4] one in the scala vestibuli and one in the scala tympani, with an appropriate associated electronic circuit that limits the electrical area to which the electrodes are sensitive to 1 to 3 mm of the organ of Corti. Their

conclusions, however, have ignored certain experiments of the past, and have been based upon the use of the differential-electrode technique which, itself, has a sufficient number of inherent drawbacks to warrant a careful examination of these procedures.

It is the primary purpose of the experiments to be described here to compare these techniques and to reveal just how accurate a picture the round-window electrode gives of organ-of-Corti activity. Secondarily, the experiments have been designed to investigate, once again, the patterns of vibratory response along the basilar membrane, and to suggest the locus of the so-called "sharpening mechanism."

METHOD

The techniques of recording the electrical potentials of the cochlea will be described specifically along with the individual experiments. In all instances the manner of stimulation remained the same.

Each guinea pig, the animal used throughout, was deeply anesthetized with an appropriate intraperitoneal dosage of a solution of diallylbarbituric acid with urethane. A postauricular incision was made and was extended ventrally around the angle of the mandible to a point just medial to and half way along the body of the mandible. The masseter and body of the mandible were cut through and the posterior portion removed, leaving the bulla and mastoid region exposed. The bone of the bulla and mastoid was removed with care that the tympanic ring was not broken thus exposing the round window and entire length of the cochlea so that electrodes could be placed on the round window and various turns of the cochlea either separately or simultaneously.

The experiments were carried out in a sound-proof, electrically-shielded room. The sound was conducted to the animal's ear through a hard rubber tube which was connected to a loud-speaker driver unit (W. E. 555) mounted outside the shield on the sound-proof room wall. The hard rubber tube was terminated by a smaller diameter one that was tied securely into the external auditory meatus of the guinea pig. A concentric probe tube attached to the face of a calibrated W. E. 640AA microphone monitored the sound pressure and was used to obtain the data from which the strength of the stimulating sound in dynes per sq cm was obtained.

The electrical response picked up from the animal was fed into a Tektronix type 122 preamplifier used either with differential or single-ended input depending upon the type of electrode used. The

amplification of this unit was exactly 1000 times at all frequencies so the output read by means of a G. R. type 736-A wave analyzer could be expressed in terms of microvolts at the recording electrode.

The wave analyzer acts as a selective voltmeter tunable to any frequency from 0 to 16,000 cps with a band width of six cycles. It achieves this selectivity by combining the output of a variable frequency oscillator with the incoming signal so that the sum of the two is always at 50,000 cps. This signal is passed through crystal filters, rectified and metered. By picking up the 50 kc signal immediately after the filters it is possible to utilize practically the entire 60 db range of the early analyzer stages. Amplifying this signal and sending it through a Sound Apparatus Company model SL-4 recorder the response from the animal can be monitored continuously with a usable range of 60 db. In addition to response-voltage measurements made at several frequencies in the usual way on the wave analyzer, the continuous-running response for different frequencies was made on the recorder while various alterations and types of electrodes were surgically introduced into the inner ear.

The use of the limited-band-width wave analyzer eliminates any nerve-action potentials from the response as well as general interference arising from random body potentials of the animal.

RESULTS

In a normal inner ear sound vibrations set up along the basilar membrane a pattern of response the characteristics of which vary with frequency. These characteristics consist of differences in amplitude and phase of vibration of different regions along the membrane. The low frequencies vibrate maximally a broad region extending from the apical end of the basilar membrane. As the frequency is raised the region of most vigorous activity becomes narrower and the center of action moves toward the basal end. Such patterns have been viewed optically[5] and inferred from measurement of the cochlear potentials measured at the round window.[6] The areas of response to any frequency are conceded to be too broad for there to be any strict place of action for specific frequencies. Furthermore, although the region of maximum response moves toward the basal end with increasing frequencies, all tones apparently utilize, to some extent, the entire length of the organ of Corti; thus the regions for different frequencies overlap. As was pointed out by Wever and Lawrence[7] and earlier by Wever,[8] the linear relationship between the cochlear response and stimulating sounds of increasing intensity requires the interpretation

that all tones activate all hair cells at all intensities, but not necessarily to an equal degree. As the stimulating tone is increased in intensity the region of maximum activity becomes broader and broader, the lows spreading down to the basal region and the highs on either side of their maximum. When the ear is overstimulated by a pure tone a relatively broad region of organ of Corti at and surrounding the area of maximum activity is damaged. Since responses to other tones also utilize this area it is to be expected that sensitivity to the other driving frequencies would also be lost.

If a single electrode placed anywhere on the cochlea registers the electrical potentials from all hair cells in response to all frequencies the recordings should show a general loss. If a round window electrode records from only the basal half of the basal turn it should show a loss only if this region has been damaged. A pair of "differential" electrodes that records from only a limited region should show a severe loss for the frequency producing the injury providing the electrodes could be placed precisely in the middle of the damaged area. This area may not be in exactly the same locus for different animals so it is not possible to be so precise in the electrode placement, a fact which constitutes the major drawback in the use of pairs of "differential" electrodes. They also do not record the response outside their region of coverage and so do not indicate the activity which the stimulating tone, if strong enough, does activate.

These considerations leave three questions which are the basis of the following experiments and must be answered before one can be certain the round-window electrode gives an accurate picture:

1. Does the method of recording from a restricted area by means of a pair of "differential" electrodes give any information not in accord with the patterns of activity as interpreted from a round-window electrode?

2. Do single electrodes placed in different regions of the cochlea present different patterns of loss than does the round-window electrode?

3. From how much of the organ of Corti from base to apex does a round-window electrode record?

Comparison of Responses Recorded from Paired "Differential" and from a Single Round-Window Electrode. The characteristic of a pair of electrodes that make them "differential" and thus restricted in their coverage is that any signal that arrives in phase at the two

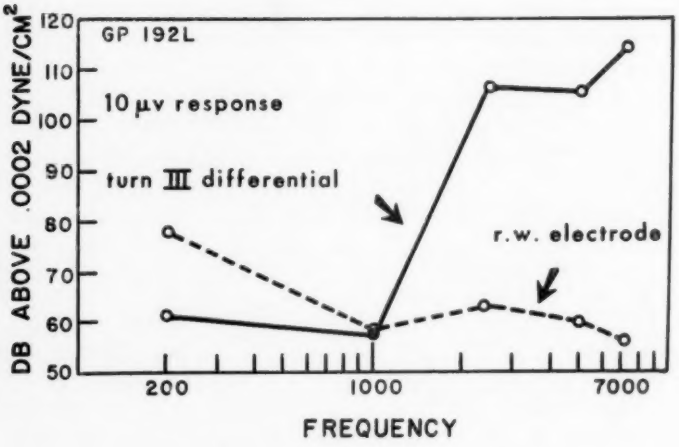


Fig. 3.—Sensitivity curves indicating the amount of sound necessary at various frequencies to produce 10 microvolts of response in the cochlear potentials when recorded by two different techniques.

pick-up points is electronically cancelled out. Only those signals that are more positive or negative at one electrode than at the other are recorded. If these two electrodes are inserted, for example, in the third turn of the guinea pig's cochlea (there are approximately 4½ turns) potentials that originate in the basal region will arrive at the pick-up points practically in phase and be cancelled out, thus the higher frequencies will not be recorded. This is the result reported by Tasaki, Davis and Legouix[4] from which they concluded that the high tones do not utilize the more apical regions when intensity is increased. But in this experiment they did not measure potentials of less than about 10 microvolts in the apical turns. If the active region for high tones spreads more and more with increasing intensity as has been interpreted from round-window recording experiments one would expect there to be a small amount of potential produced from the hair cells in the restricted recording region of the "differential" electrodes in the third turn.

Figure 3 shows the results of an experiment designed to find out how much sound is necessary at various frequencies to produce 10 microvolts of response when recorded simultaneously on the same animal by the two techniques in question. At 200 cps the "differential" electrodes require about 18 db less sound than does the round-

window electrode. This is to be expected because turn 3 is closer to the region of maximum activity for low frequencies than is the round window. At 1000 cps both types of electrodes require the same amount of sound. At higher frequencies the "differential" electrodes are extremely insensitive as compared with the round-window electrode but they do record a response. The round-window electrode is more sensitive because the region of activity is moving closer with increasing frequency. If the "differential" electrodes are pulled out of the cochlea and left in the open air, or are placed in some adjacent tissue nothing is recorded. One can conclude only that the pattern of response to the higher frequencies has actually spread to the third turn. This means it is possible for there to be a response to high tones even if the basal region were damaged providing the stimulus intensity is great enough.

The above characterizes the relative sensitivity of the ear to various frequencies up to the point of generation of potentials. Further information is gained by studying the growth of electrical response as the stimulus intensity is increased. As the intensity of the tone is increased the magnitude of the response, as recorded by a round-window electrode, increases proportionally up to a point. This relationship at some particular high intensity then becomes nonlinear, the response only increasing a portion of that of the sound intensity increase. Finally a maximum is reached. A detailed discussion of this function is given in Wever and Lawrence.[7] Presumably in the linear region all hair cells are responding linearly. As the stimulus intensity is increased further the region of organ of Corti undergoing the most vigorous action begins to fail in its ability to produce more response so the total potential increases are no longer proportional. Finally, an intensity is reached at which the hair cells in this region begin to give a diminished response which may just equal the output from adjacent hair cells (the maximum response) and finally exceed this output (the decreasing portion).[9]

Since the round-window electrode records from all portions of the cochlea (or from the lower half of the basal turn?), it is important again to know if "differential" electrodes give any different picture of these input-output functions not interpreted from recordings at the single basal position.

Figure 4 shows intensity functions recorded for three different frequencies from two different animals. For each animal the round-window recording was made first, then the "differential" electrodes were placed in the scala tympani and scala vestibuli of the third turn,

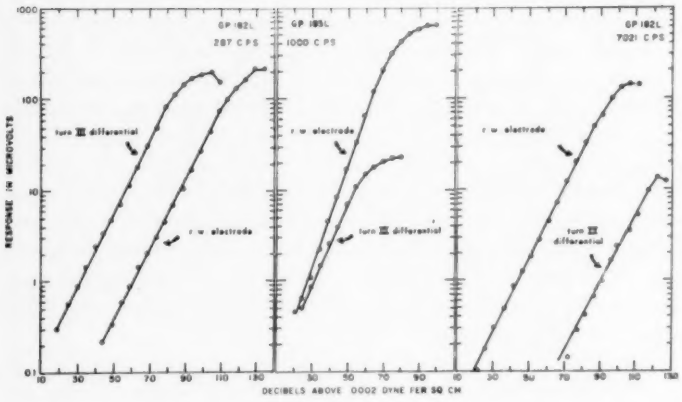


Fig. 4.—Intensity functions at various frequencies showing the increase in cochlear potentials as sound input is raised (input-output functions) when recorded by two different techniques. For each frequency the round-window recording was made first, the turn III "differential" next, and then the round-window record repeated. For 287 cps and 7021 cps the repeat round-window recording was identical to the first, but for the 1000 cps the repeat round-window recording fell below the differential-electrode recording indicating that the change in slope and maximum of the differential-electrode record is related to an injury produced by the electrode. For general sensitivity and intensity measures "differential" electrodes reveal no more than single electrodes and may introduce indeterminate factors.

an intensity function taken, and, finally, the round-window recording repeated. The general form of the functions is the same for both methods.

At 287 cps the intensity functions for both methods are practically identical except that the turn three "differential" electrodes take less sound for a given response. This was also seen in Figure 3 and indicates only that these electrodes are nearer the major source of the potentials. The departure from linearity and maximum occur at very nearly the same response level in both cases. When the round-window reading was repeated the response function fell on the same points as before.

At 7021 cps the round-window electrode is the more sensitive as was seen in Figure 3. Here the value of sensitive recording is revealed. Practically the entire function recorded by the third turn "differential" electrodes is below 10 microvolts, but it is all a linear

function. The only portions above 10 microvolts are the nonlinear and maximum regions of the function. If nothing less than 10 microvolts is recorded the impression could easily arise that "differential" electrodes reveal that the third turn response to the high frequency is of a different form than that recorded at the round window. However, the response is just what would be expected from patterns of response revealed by round-window recording. Repeat of the round-window response after placement of the "differential" electrodes again fell on the same points.

The round-window response to 1000 cps shows a normal function but the turn three "differential" electrode recording shows a different slope below 10 microvolts. In Figure 3 the turn three "differential" electrode and the round-window electrode were equally sensitive at 1000 cps but in this figure at 10 microvolts they differ by about 8 db. This suggests that the introduction of the "differential" electrodes in this animal produced some injury to the structures of the scala media, changing the sensitivity, the slope and the maximum. This was borne out by the fact that a repeat of the round-window response after the differential recording had been made revealed a response much smaller than previously.

From these results of Figures 3 and 4 it can be concluded that the use of "differential" electrodes gives no more information than a round-window electrode and has in addition the following disadvantages:

a. The electrodes cannot be placed with certainty in the region of maximum organ of Corti activity for any particular frequency, and their placement is anatomically limited to only certain regions.

b. Their placement may cause unknown injury producing a strange pattern of response that is entirely the result of this injury.

c. No information is revealed concerning the activity of regions adjacent to the restricted-recording area of the electrodes.

Comparison of Single Electrodes Placed in Different Regions of the Cochlea. As mentioned earlier the results of Figure 2 were recorded through a platinum-foil electrode on the round-window membrane and an indifferent electrode in the temporalis muscle. Because of attenuation of the potentials as they pass through the fluids of the inner ear and because the pattern of activity shifts as the stimulating frequency changes, single electrodes at different distances from the base of the cochlea along the basilar membrane should favor the re-

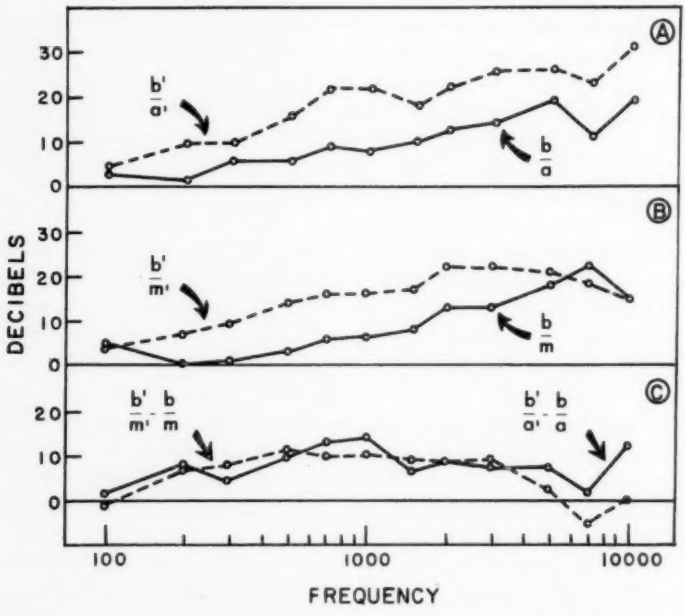


Fig. 5.—Comparison of sensitivities for various frequencies as recorded by single electrodes at the base (b), second turn (m) and apex (a). Curves b/a and b/m represent the number of decibels by which the basal electrode is more sensitive than the other, i.e., how much less sound is required to produce a given response at one electrode position as compared with the other. Curves b′/a′ and b′/m′ represent the same sensitivity comparisons following overstimulation of the animals' ears with 1000 cps at 122 db above .0002 dyne/cm^2 for 7 minutes. The basal electrode becomes relatively more sensitive but there is no specific frequency shift. In graph C the differences in sensitivity before and after overstimulation are compared. Any differences in sensitivity at 1,000 cps revealed by the three electrode positions should show up as differences in these curves. b′/m′ - b/m and b′/a′ - b/a are practically identical. It is apparent that the general frequency loss following pure-tone overstimulation is not a characteristic of electrode position.

sponse for different frequencies. The following experiments were carried out to determine this and the extent to which the general-loss audiogram of Figure 2 is affected by different single-electrode positions.

Four guinea pigs were prepared at separate times as described earlier. An indifferent electrode was placed in the temporalis muscle and three recording electrodes were placed at different distances from

the base of the cochlea. One electrode (b), a platinum-foil, was placed on the round-window membrane, a second, a steel needle, on the second turn (m), and a third, also a needle, as near the apex as possible (a).

The amount of sound necessary at 12 different frequencies (100, 200, 300, 500, 700, 1000, 1500, 2000, 3000, 5000, 7000, and 10,000 cps) to produce a constant response of 3 microvolts was first determined. Because the bony wall of the cochlea reduces the magnitude of the response considerably the round-window electrode always requires much less sound at the various frequencies to produce 3 microvolts than the other, needle, electrodes, and since the locus of activity as frequency is raised moves toward the base, this better round-window response becomes increasingly greater as the frequency gets higher. The amount of sound required at one of the needle-electrode positions can be subtracted from that at the round-window position and the amount by which the round-window electrode is better than the others for the different frequencies can be plotted.

The results of the four animals were averaged and are plotted in Figure 5. In graph A the line b/a represents the amount in db by which the round-window electrode (b) is better (requires less sound for 3 microvolts) than the apical electrode (a), and in graph B the line b/m represents the amount in db by which the round-window electrode is better than the middle electrode (m). These results are practically identical with others that have been published previously[7] and show the increasing advantages of the round-window electrode, as frequency is raised, over both the apical and middle electrodes.

After these initial recordings were made the ears of the animals were stimulated with 122 db above .0002 dyne per sq cm for 7 minutes as in Figures 1 and 2. Following this, 3 microvolt sensitivity curves for the different electrode positions were again taken. An injury caused by a specific frequency at a certain characteristic location should show up differently for different electrode positions. However, such a difference was not observed. In Figure 3, graph A, the line b′/a′ represents the amount in db by which the round window electrode (b′) is better than the apical electrode (a′) after overstimulation, and in graph B the line b′/m′ represents the amount in db which the round-window electrode is better than the middle electrode (m′). Still the round-window electrode takes less sound to produce the 3 microvolt curve than the other electrode positions except for the lower-most frequency where the difference is only about 3 to 4 db.

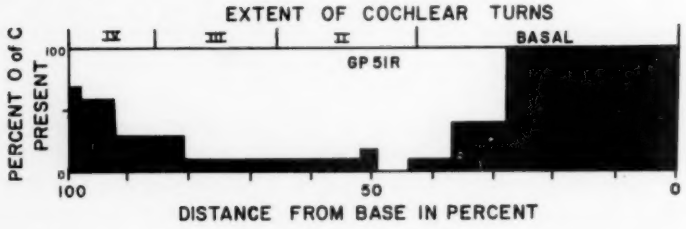


Fig. 6.—A reconstruction of the per cent of organ of Corti present (black area) after 56 days of recovery following overstimulation of a guinea pig's ear by white noise at 136 db above .0002 dyne/cm^2 for 20 minutes. Extent of each cochlear turn is shown above and the per cent distance from the basal end shown below. Almost two-thirds of the basal turn was histologically normal. See electrical audiogram in Figure 7.

It is to be expected that if the 1000 cps overstimulation caused a localized damage to the organ of Corti at a specific point the electrode nearest the region of injury would show a sensitivity curve different than would the more remote electrodes. This should show up in the difference between the base-apical or base-middle electrode curves before and after the overstimulation. The differences between these two sets of curves are plotted in graph C of Figure 3 and the resulting curves show a marked similarity. This indicates that the generalized loss following a pure-tone overstimulation is not a function of electrode placement. A single electrode placed anywhere along the cochlea shows the same general loss for all frequencies. The general loss shown by a round-window electrode is then no argument in support of the contention that this placement records from only the basal half of the basal turn of the cochlea.

The important question remains, then, as to how sensitive the round-window electrode is to changes in various parts of the cochlea. This can be studied by the destruction of particular parts of the organ of Corti by overstimulation or by actual surgical damage.

Effect of Specific Lesions on Round-Window Recording. In the course of another experiment[10] several guinea pigs were stimulated with high levels of noise. After stimulation the animals were allowed to recover over a period of 56 days at which time they were perfused intravitally and sacrificed for histologic processing and microscopic study of the temporal bone. Many showed extensive loss of the organ of Corti for the upper turns with a perfectly normal appearing area in the basal turn extending to the very end of the base.

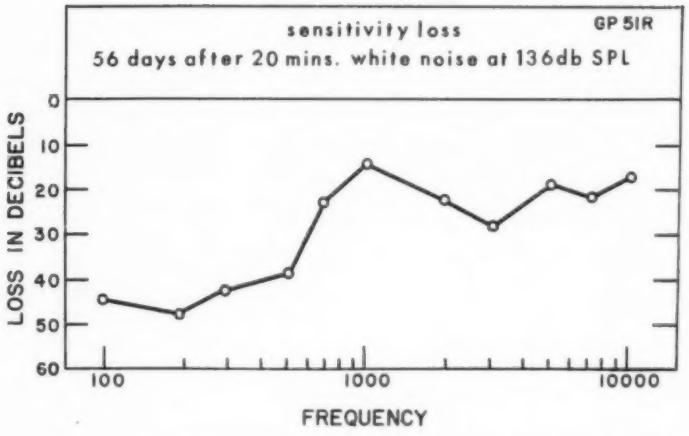


Fig. 7.—The loss in sensitivity to various frequencies following the indicated injury and recovery for the same animal whose per cent organ of Corti present is shown in the preceding figure. Because there is greater organ of Corti loss for the upper turns than for the basal, a greater loss for low frequencies than for the highs is to be expected. Obviously the round-window electrode by which this sensitivity shift was determined is recording potentials from the entire cochlea.

Figure 6 is a linear plot of the amount of organ of Corti remaining in an animal used in the above experiment. The data was taken from a graphic reconstruction of the prepared serial sections with the black, filled-in area indicating the per cent organ of Corti present. Because it is common practice to plot frequency going from low to high as one proceeds to the right the linear plot has been made so that the basal end is to the right. It is at this end of the cochlea that the electrode is placed and where the high tones show the region of most vigorous activity. Obviously, with such extensive damage to the top three turns, one would expect considerable loss to the low frequencies. Of course, as intensity is raised for these frequencies more and more of the basal turn will be used, so sensitivity should not be lost completely. On the other hand, since the highs utilize the base for their region of maximum activity, there should be little loss of sensitivity, but since the response pattern for the high frequencies also spreads to the upper turns there should be some loss.

If the round-window electrode records only from the lower half of the basal turn the electrical recording in this animal should appear normal.

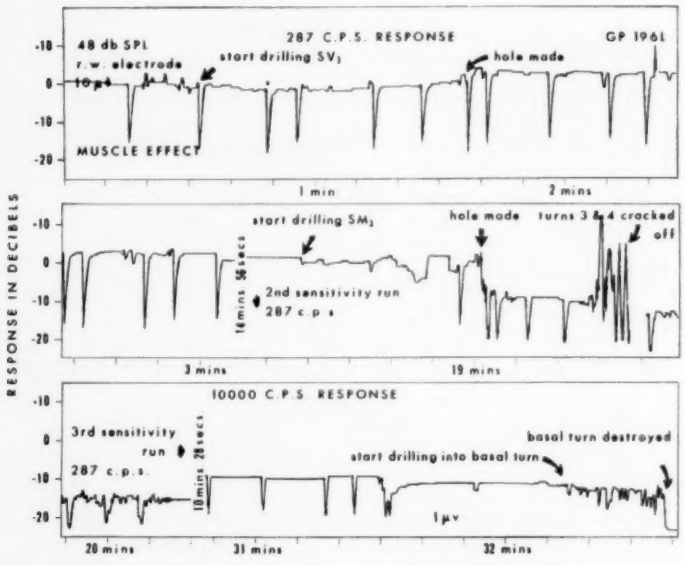


Fig. 8.—A running-time record of the cochlear potentials as recorded by a round-window electrode while the ear was stimulated by a low-intensity 287 cps tone. Surgical damage in various regions of the cochlea had the indicated effects. The sharp downward spikes are the result of attenuation in sound conduction produced by spontaneous muscle contraction. The 10,000 cps record was made to check the recording for artifact; destruction of the basal turn eliminated the response. The periodic sensitivity runs are shown in Figure 9.

In Figure 7 the amount of loss for the various frequencies produced by the anatomic damage represented in the preceding figure and recorded by a round-window electrode is shown. Exactly the kind of loss is shown that would be predicted if the round-window recording reflects the pattern of activity over the entire length of the basilar membrane. For frequencies from 100 to 500 cps there is a loss of about 45 db while above those frequencies the loss is only around 20 db.

The above experiment has the advantage of producing the damage to the organ of Corti from within so that the results are not confounded by damage to other structures that might cause loss of intracochlear fluids. It is also possible to produce restricted regions of

damage to the organ of Corti by surgical means and record the response before any loss of fluid has caused secondary damage.

In a very carefully performed investigation Walzl and Bordley[11] did just this sort of experiment. Operating on the anesthetized cat with a binocular dissecting microscope, the bone over selected portions of the spiral ligament was removed with a small dental burr. The spiral ligament was loosened by light pressure with a blunt needle which damaged the organ of Corti in this restricted region. When this procedure was successful there was no rupture of either Reissner's or the basilar membranes, no escape of endolymph, and no hemorrhage into the cochlear duct. Both before and after this experimental injury the cochlear responses, recorded by a single silver wire at the edge of the round window, were measured for a wide range of frequencies. Afterwards the animals were all prepared for histological study and graphic reconstructions made of each cochlea so that the locus of the experimental lesion could be accurately determined in terms of distance from the basal end of the basilar membrane.

High tone losses were caused by basal lesions while low tone losses were caused by more apical ones. Extreme apical lesions when small did not affect sensitivity to weak sounds but when the damaged area was enlarged there was a general loss for all frequencies. When the injury was localized at a point about 66 per cent of the extent of the membrane above the basilar end there was produced a shift in sensitivity to 256 cps of about 20 db with more moderate losses up through 724 cps. Small local lesions produced slight losses to specific higher frequencies but larger areas of injury resulted in impairment of sensitivity to all tones above 512 cps.

Whenever a specific frequency showed a loss of sensitivity because of a complete injury in a restricted area, the loss amounted only to about 10 or 20 db. More extensive injuries caused greater losses but also spread to adjacent frequencies. All tones apparently spread their region of activity over wider and wider areas as stimulating intensity is increased.

We have repeated these experiments but with a somewhat different method of recording the responses. As described earlier the response was recorded continuously on a moving chart with a recording intensity range of 60 db which means amplifier gain never had to be switched.

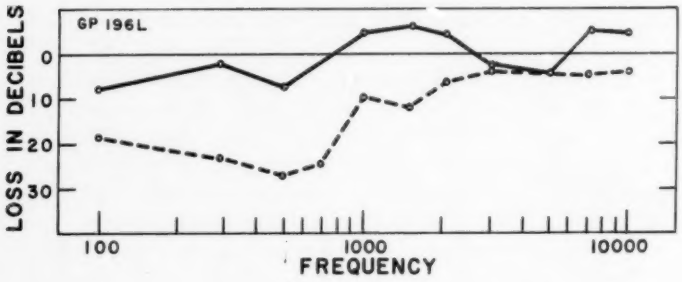


Fig. 9.—Shifts in 3 microvolt sensitivity produced by the surgical injuries shown in the preceding figure. The solid-line curve is the second sensitivity run compared with the normal (zero line) made preceding the experiment. The injuries have affected sensitivity to the very low frequencies to a slightly greater degree than to the higher frequencies. The dashed-line curve is the third sensitivity run compared with the normal. Removal of turns 3 and 4 has seriously injured the low frequencies as well as decreased sensitivity to the highs.

In the first experiment to be described an initial determination was made of the amount of sound necessary to produce 3 microvolts of response at 10 different frequencies. This served as a base line for the sensitivity measures made later. The running-time records then followed.

In Figure 8 the continuously-recorded response to 287 cps is shown. The sound was first set at an intensity that gave the relatively low response of 10 microvolts. As indicated in the figure this required a sound pressure level 48 db above .0002 dyne per sq cm. While the response was being recorded a small hole was drilled in the scala vestibuli of the third turn. One of the reasons for drilling a hole in the scala vestibuli was to see if the insertion of electrodes by this means had any particular effect upon responses of the cochlea. Obviously such a hole had no effect upon this low-frequency response. At the end of 14 minutes 56 seconds a second 3 microvolt sensitivity measure was made for the 10 frequencies. This is shown as the solid line in Figure 9. The overall response is somewhat erratic with no particular pattern of loss being revealed.

The running-time record was then continued and as indicated in Figure 8 a hole was drilled in the scala media of the same turn. The instant the hole was made, which had the effect of destroying the

organ of Corti in this region, there was a loss of sensitivity amounting to about 10 db. Cracking off completely the third and fourth turns reduced the response another 5 db to a level of about 1.7 microvolts. At this time another sensitivity measure was made for the same 10 frequencies and is shown as the dashed line in Figure 9. Now there is a loss of 20 to 30 db for the low frequencies up to 700 cps. Above this frequency there is gradually less loss until at 10,000 cps it amounts to about 3 db.

It is obvious that the round-window electrode must be recording potentials from the organ of Corti at least through the third turn and that the third and fourth turns are necessary for maximum sensitivity of low tones up to at least 700 cps and that these turns contribute something to the sensitivity of the cochlea to higher frequencies.

In order to check that these effects were not the result of the electrode recording something other than the cochlear response, the response to 10,000 cps was taken as the running-time record continued for the next minute and a half with the electrode still in the same position. This frequency was used because it seemed to be the one least affected by the destructive procedure. While this record was being made the basal turn was destroyed and the response dropped to the noise level of the amplifiers indicating that our electrode was not recording artifact.

The above records were made at low-response levels with the region of vigorous activity of the basilar membrane small so that the limited lesion to the organ of Corti showed a relatively great effect on sensitivity to certain frequencies. The next record was made at a higher-response level so that a greater spread of major activity along the basilar membrane would be involved. In this case small lesions should have a less noticeable effect.

Again before proceeding with the running-time record a sensitivity measure was made to serve as a base line for later such determinations.

As shown in Figure 10 the response was set at 100 microvolts which required, at 287 cps, a sound pressure of 68 db above .0002 dyne per sq cm. As the experiment proceeded drilling a hole in the scala media of the third turn with consequent injury to the organ of Corti had no effect nor did cracking of the fourth and part of the third turns. However, an injury to the sensory area in the second turn and breaking off the rest of the third turn reduced the response about 12 db, to a level of 25 microvolts.

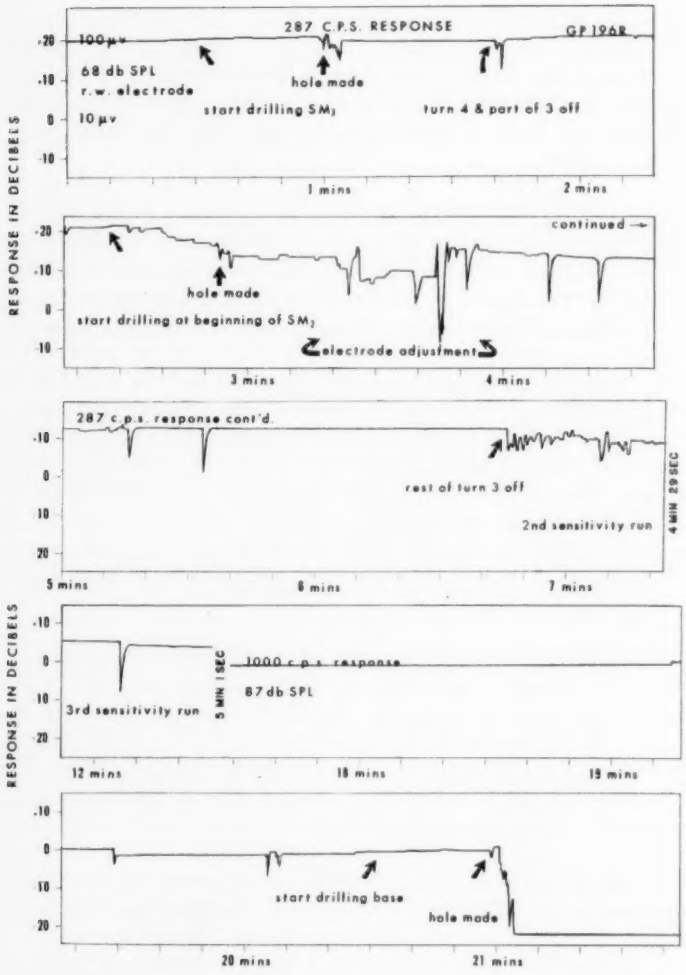


Fig. 10.—A running-time record of the cochlear potentials as recorded by a round-window electrode while the ear was stimulated by a high intensity 287 cps tone. These results are to be compared with those of Figures 8 and 9 in which a low intensity stimulus are used. Surgical damage in various regions of the cochlea had the indicated effect. Injury to turns 3 and 4 has less effect when stimulus intensity is high. The 1,000 cps record was again made to check the recording for artifact; destruction of the basal turn eliminated the response. Note that the response scale is shifted beginning with the middle record.

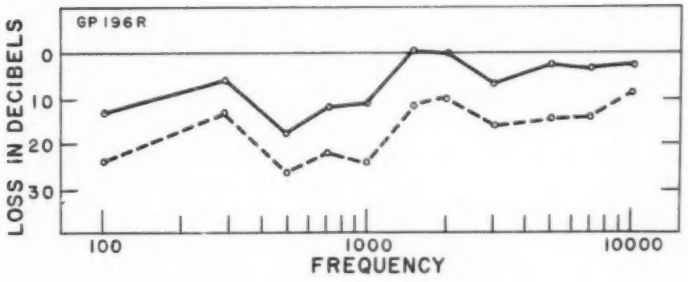


Fig. 11.—Shifts in 3 microvolt sensitivity produced by the surgical injuries shown in Figure 10. The solid-line curve is the second sensitivity run compared with the normal (zero line) made preceding the experiment. Again, injury to the upper turns produces a greater loss for the lows than for the highs. The dashed curve is the third sensitivity run showing the general deterioration to all frequencies following the drastic surgical trauma.

After removing the third turn a second sensitivity measure was made and is shown as the solid line in Figure 11. This again was a 3 microvolt measure and shows a greater loss for the low frequencies than for the highs. In order to show the general deterioration that follows such drastic damage to the cochlea a period of approximately 10 minutes was allowed to elapse and another sensitivity run made. This latter is shown as the dashed line in Figure 11. The frequency characteristics have remained the same but the ear has lost sensitivity to all tones.

In order to check again to make sure the electrode was recording the potentials from the cochlea during this severe damage to the third and fourth turn, a record of 1000 cps was made for several minutes and then a hole made in the basal turn damaging almost completely the rest of the cochlea. The final record of Figure 10 shows the abolition of the response by this procedure.

The two preceding experiments support the observation that a round-window electrode records from the entire cochlea. A further experiment involves destruction of various parts of the cochlea to find out what regions, and how much, of the organ of Corti is involved for various frequencies. The response to 1000 cps was next tested with the response level set to the relatively high level of 100 microvolts as various portions of the cochlea were damaged. The running-time record is shown in Figure 12.

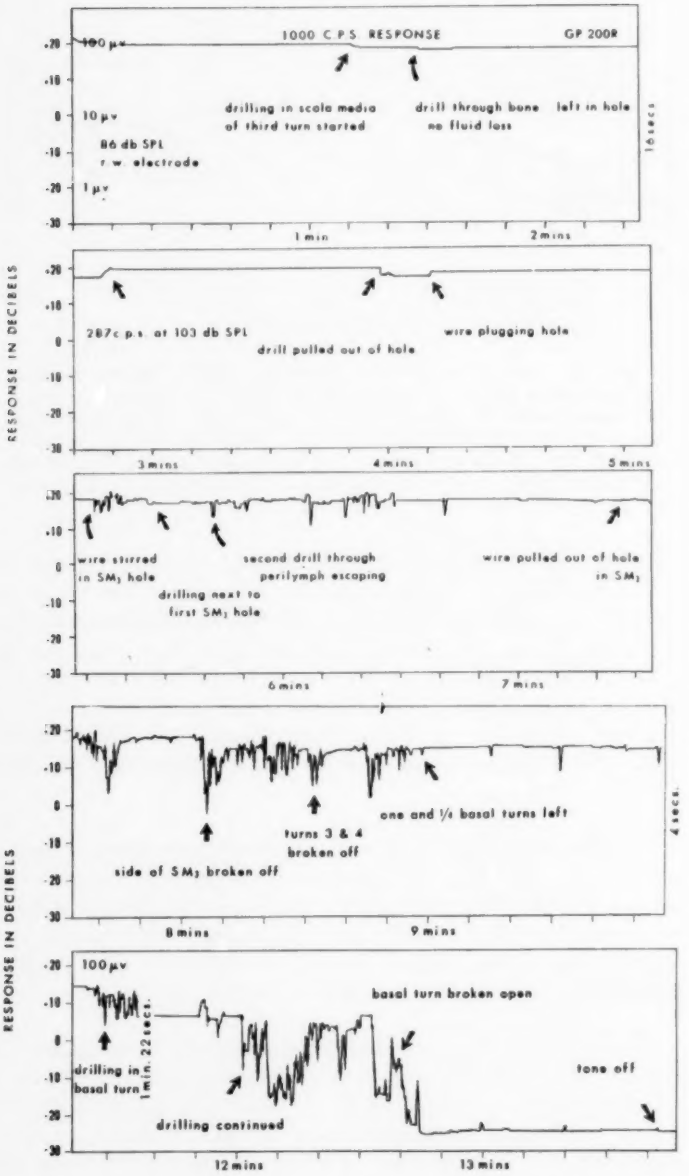


Fig. 12.—A running-time record of the cochlear potentials as recorded by a round-window electrode while the ear was stimulated by a high-intensity 1,000 cps tone. Surgical damage in various regions of the cochlea had the indicated effect but the response is down only about 6 db with 1¼ basal turns left. Opening the basal turn eliminates the response. The first, fourth, and fifth charts are records of 1,000 cps.

Drilling a small hole through the scala media of the third turn, thus damaging the organ of Corti, and leaving the minute drill in the hole affected the response only about 2 db. Because 287 cps involves the third turn more vigorously than does 1000 cps the recording was switched to 287 cps and the drill subsequently removed and replaced to determine the effect of opening the hole. There is seen only slight effect which may be related to sound transmission within the cochlea rather than to the effect of damage. Damaging the region further produced no additional loss in response as the continuation of the record in the third chart shows. This is to be expected from the results shown in Figure 10 provided the sound intensity is high enough to produce a large response by extensive cochlear activity.

In the fourth chart of Figure 12 further results are shown as the stimulus was switched back to 1000 cps. Breaking off all but 1¼ of the basal turns had a total effect of only about 6 db on this frequency which, nevertheless, means the magnitude of the potentials was cut in half. As the record continues in the fifth chart it is shown that drilling into the basal turn has a gradual effect until the basal turn in broken open, destroying just about all of the organ of Corti in this region. When this happens the response is abolished.

Figure 13 shows the results of the same type of experiment using a frequency of 7000 cps. The response was set at 7 microvolts so that the region of major activity would be small. A hole in the scala vestibuli of the third turn and breaking off the fourth turn have the just-detectable effect of about 1 db. Drilling a hole in the basal scala media about 4 mm from the basal end has the severe effect of nearly 20 db. There is, however, a residuum of response as shown in the lower chart which can only arise from areas extending beyond the region of damage. This is abolished only by destroying the entire cochlea.

COMMENT

The series of experiments just described was designed to find out whether, following a 1000 cps pure-tone overstimulation, the picture of a general-sensitivity loss to all frequencies as determined by measures of the electrical response of the cochlea was an accurate one or the result of the technique in which a round-window electrode is used. Two other questions have concerned us: if the electrical recording is accurate how can the discrepancy between this and audiometric measures be accounted for, and if the electrical recording really only reflects some characteristics of the round-window technique just what are the limitations of this technique?

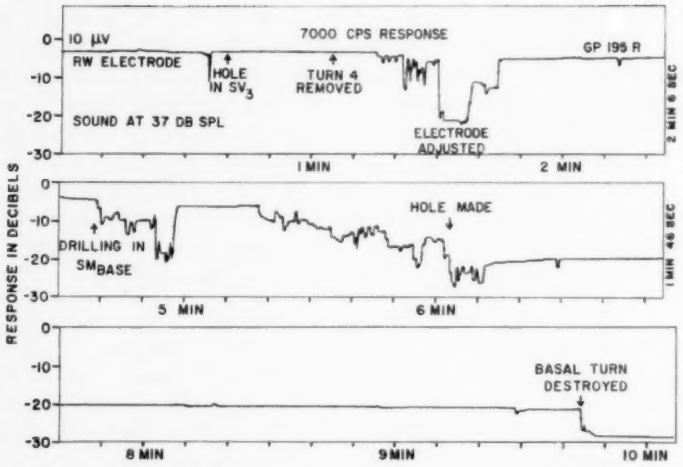


Fig. 13.—A running-time record of the cochlear potentials as recorded by a round-window electrode while the ear was stimulated by a low-intensity 7,000 cps tone. Surgical damage in various regions of the cochlea had the indicated effect. Removing the fourth turn had little influence on the response while a hole in the basal scala media reduced the response about 17 db. The response to this frequency could be abolished only by destroying the entire basal turn.

It is obvious from the results of the reported experiments that claims that a round-window electrode records only from the basal half of the basal turn are unfounded. Evidence that such a method of picking up potentials actually records from the entire cochlea can be found in many past experiments already referred to and these are completely substantiated by the histological evidence and running-time records during surgical destruction reported here.

Use of intracochlear "differential" electrodes for the recording of overall frequency response only confuses the picture by recording from isolated areas of the organ of Corti whose position with respect to any region of damage is unknown. The insertion of such electrodes can also produce indeterminate damage which may alter both the low-level sensitivity and the response to higher intensities or either of these separately. The experiments described here show that this is so and that the "differential" electrodes give no more information than a round-window electrode. They do show differences in sensitivity in accordance with the frequency in use and position of elec-

trodes along the organ of Corti. These differences, however, are the same as shown by single electrodes and can be easily accounted for, but the property of recording from a limited area, as "differential" electrodes do, has a virtue in that the electrodes can and have been used[4] to confirm the mechanical patterns of response along the basilar membrane as pictured earlier both optically and electrically.

We must conclude that the electrical measure of Figure 2 is accurate except that the low frequencies are progressively favored over the higher frequencies because of the position of the round-window electrode. Paired "differential" electrodes do not reveal a different picture because they cannot do so when they record from a limited region of only 1 to 3 mm of organ of Corti. Even several pairs in different turns can only be placed in certain locations because of the anatomical situation and so do not record all cochlear activity. Single electrodes placed in different turns favor the frequencies whose region of major activity lies the closest, but such electrodes give no different electrical audiogram when this sensitivity difference is accounted for than does a round-window electrode.

One of the reasons that the round-window electrode seems to record only from the basal turn is that it is in the basal turn that most of the action takes place. All tones are activating to some extent the sensory cells of the basal turn, and as intensity of the stimulating tone is increased this activity becomes more vigorous. Another fact, often overlooked, is that, as shown for the guinea pig in Figure 6, the basal turn contains between 40 and 50 per cent of the entire extent of the organ of Corti.

In order to determine this figure more accurately the graphic plots of 36 separate guinea pig ears that were used in the study from which Figure 6 was taken were retabulated and averaged in terms of the per cent of organ of Corti found in each turn of the guinea pig cochlea. The following are the figures obtained:

Basal turn	49%
Turn II	22%
Turn III	18%
Turn IV	11%

If all sensory cells were activiated equally and an electrode recorded the sum of their aroused potentials, the basal turn would account for almost 50 per cent of the maximum voltage output. In other words the top three turns could be destroyed and there would be a theoretical loss of only 6 db. It is apparently only at threshold levels that

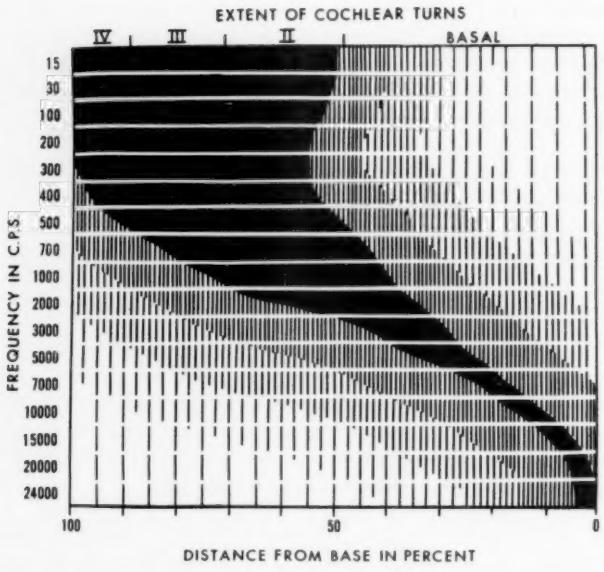


Fig. 14.—A diagrammatic representation of the spread of response for a number of frequencies within the audible range. The density of the inking for any frequency indicates the relative degree of activity with the solid black denoting the region of greatest amplitude. These data were taken from experiments summarized by Wever.[8] Data on the spread of response were obtained from electrical recordings and surgical injury experiments; all tones utilize the entire basilar membrane to some extent. The data on per cent of basilar membrane in each turn, indicatd at the top of the figure, were obtained from histological reconstruction of 36 guinea-pig cochleae. The basal turn includes 49 per cent of the entire length of basilar membrane. Per cent distance from base to apex is plotted right-to-left because frequency increase is usually shown as progressing to the right.

the upper turns become important because then, although the spread is still broad, the region of major action is small. At this level all sensory cells are not vibrated to an equal extent.

To illustrate this a map of the region of organ of Corti activated maximally by certain tones together with an indication of the extent of spread of activity is shown in Figure 14. This map of activity was constructed from the data on experiments summarized by Wever,[8] and the percentage of organ of Corti in each turn is the data presented above. The black bars show the area of maximal activity for each frequency and the vertical bars show the spread of action: the denser

the number of bars the more vigorous the activity. It can be seen that frequencies above 500 cps all have some of their maximal activity region in the basal turn, and from the data of differential-electrode experiments and those on surgical destruction reported here, it would appear that the lower frequencies may spread into the basal turn more than indicated.

An electrode at the basal end of the cochlea thus gives an accurate picture of the accumulated activity where every tone uses the area occupied by the major activity region of others, and so a destruction of a certain region shows a loss to a broad band of frequencies.

To account for the discrepancy then between Figure 1 and Figure 2 we must search elsewhere than along the organ of Corti. The effect of sharpening the frequency of loss must be looked for in a more central process, starting with the way in which the neural system "interprets" the pattern along the basilar membrane. And it would appear that Békésy[12] has provided the inchoate idea in his recent magnificent discussion of "funneling" in the nervous system. The so-called sharpening mechanism for frequency analysis does not lie on the basilar membrane nor in the nerve but in the interaction of the two. The initiating processes of this must be looked for in the diffuse innervation of the organ of Corti.

We see one consequence of this process in Figure 1 where the threshold shift has occurred at a frequency approximately one octave above the stimulating frequency. This may well be the indication that the organ of Corti has been affected at these high levels of stimulation because, as has been pointed out before,[13] the threshold shift, temporarily produced by low intensity levels, shows up audiometrically at the stimulating frequency but does not show up at all in the cochlear potentials. This neural "interpretation" of organ-of-Corti damage may also account for the so-called 4096 dip usually seen as the first sign of a noise-induced hearing loss. Figure 14 shows 2000 cps to have its region of maximum activity centered at the 50 per cent point along the basilar membrane. This indicates that the area is in constant use to some extent by all frequencies throughout the audible spectrum. A gradual deterioration of the organ of Corti in this 2000 cps region would register audiometrically as a hearing loss at 4000 cps.

SUMMARY

1. The question has been raised in this report as to why, after overstimulation of the human ear with a 1000 cps pure tone, the

threshold shift should show a sharp frequency loss an octave above the stimulating frequency, whereas when a guinea pig ear is overstimulated with the identical level and duration of a pure tone the electrical responses of the cochlea show a general loss to all frequencies. Two possibilities are suggested: the sharp frequency shift shown audiometrically is the result of neural "interpretation" of organ-of-Corti damage, or the general-frequency loss seen in electrical recording from the cochlea of an experimental animal is an artifact of the recording technique. The investigations reported here have centered around this latter point to find out whether such electrical recordings are accurate.

2. Three recording techniques are studied and compared: paired "differential" electrodes, single electrodes, and a round-window foil electrode. It is concluded that:

a. Paired "differential" electrodes do not present any clearer picture of cochlear response loss after overstimulation than does a round-window electrode for the following reasons:

   1. They cannot be placed with certainty in the region of maximum organ-of-Corti activity for any particular frequency and their placement is anatomically limited to only certain regions.

   2. Their placement may cause unknown injury producing a strange pattern of response that is entirely the result of this injury. This is particularly true at the higher-intensity levels where the injury may change the slope of the input-output function or lower the maximum.

   3. No information is revealed concerning the activity of regions adjacent to the restricted recording area of electrodes.

b. By comparing single electrodes placed in different turns and by selective destruction of regions of the organ of Corti it is shown that a round-window foil electrode records potentials arising over the entire length of cochlea but, because of the electrical attenuation within the fluids, records weaker apical responses than basal ones. This, however, is a graded attenuation, can be predicted, and does not change the general frequency loss pattern of the electrical response.

3. Following a pure-tone overstimulation the discrepancy between the sharp frequency shift revealed audiometrically and the broad general frequency loss shown by electrical recording is real and not a result of technique.

4. From these experimental observations it is apparent that the sharp frequency analysis in the hearing process does not occur on the basilar membrane nor strictly in the auditory nerve system but in an interaction of the two. It is to be looked for in the way the diffuse innervation of the sensory cells "interprets" the characteristic broad responses along the extent of organ of Corti.

4506 KRESGE MEDICAL RESEARCH BUILDING

REFERENCES

1. Wever, E. G., and Smith, K. R.: The Problem of Stimulation Deafness: I. Cochlear Impairment as a Function of Tonal Frequency. Jour. Exper. Psychol. 34:239-245, 1944.

2. Davis, H.: Biophysics and Physiology of the Inner Ear. Physiol. Rev. 37:1-49, 1957.

3. Tasaki, I.: Hearing. Ann Rev. Physiol. 19:417-438, 1957.

4. Tasaki, I., Davis, H., and Legouix, J. P.: The Space-time Pattern of Cochlear Microphonics (Guinea Pig), as Recorded by Differential Electrodes. Jour. Acoust. Soc. Amer. 24:502-519, 1952.

5. Békésy, G. v.: Über die Resonanzkurve und die Abklingzeit der verschiedenen Stellen der Schneckentrennwand. Akustische Zeits. 8:66-76, 1943. Translated into English in Jour. Acoust. Soc. Amer. 21:245-254, 1949.

6. Wever, E. G., and Lawrence, M.: The Patterns of Response in the Cochlea. Jour. Acoust. Soc. Amer. 21:127-134, 1949.

7. Wever, E. G., and Lawrence, M.: Physiological Acoustics, pp. 300-316, Princeton University Press, Princeton, New Jersey, 1954.

8. Wever, E. G.: Theory of Hearing, p. 257, p. 273, John Wiley & Son, Inc., New York, 1949.

9. Lawrence, M.: Functional Changes in Inner Ear Deafness. Trans. Amer. Otol. Soc., 1958, and ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY 68: 802-823, 1958.

10. Lawrence, M., and Yantis, P. A.: Individual Differences in Functional Recovery and Structural Repair Following Overstimulation of the Guinea Pig Ear. ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY 66:595-621, 1957.

11. Walzl, E. M., and Bordley, J. E.: The Effect of Small Lesions of the Organ of Corti on Cochlear Potentials. Amer. Jour. Physiol. 135:351-360, 1942.

12. Békésy, G. v.: Funneling in the Nervous System and Its Role in Loudness and Sensation Intensity on the Skin. Jour. Acoust. Soc. Amer. 30:399-412, 1958.

13. Lawrence, M., and Yantis, P. A.: Overstimulation, Fatigue, and Onset of Overload in the Normal Human Ear. Jour. Acoust. Soc. Amer. 29:265-274, 1957.

II

POSSIBILITIES FOR THERAPY WITH ENZYMES

Sol Sherry, M.D.

St. Louis, Mo.

The use of enzymes as therapeutic agents is a relatively new development although the concept is quite old. Robert Morris, a New York surgeon, wrote the following in the N. Y. Medical Journal of 1891:[1] "Something more than peroxide of hydrogen is wanted for managing the abscess cavities of tuberculous bone disease to our entire satisfaction. It is true that with hydrogen peroxide at hand we can open the biggest of cold abscesses in a feeling of security for the patient, and yet it is desirable to get the tough lining membrane of fibrinous lymph and the loose coagula and the sloughing diseased tissues out of the way as thoroughly as possible, for once these substances have begun to seethe in fermentative processes, we are hard pressed to keep the patient out of trouble.

"The sharp spoon and scissors will do the work, to be sure, but only after tedious labor and egregious wounding of the weak patient."

Morris then went on to describe how he used acidified solutions of pepsin, and neutral solutions of pancreatic enzymes in the treatment of tuberculous abscesses, and suggested that this type of therapy deserved further study. Despite occasional flurries of interest in the use of enzymes over the next half century, the modern era of enzymatic therapy has its origin in the period immediately following World War II, and stems from two entirely unrelated areas of interest, namely, the nature of the spreading factor in tissues, and a study of the enzymes elaborated by hemolytic streptococci. The successful

---

Presented at the St. Louis Nose and Throat Club, March 19, 1958, and at the Research and Development Section Meeting of the American Drug Manufacturers Association, October 11, 1957.

These studies have been supported by grants from the National Heart Institute, National Institutes of Health, and the Lederle Laboratories Division, American Cyanamid Co.

From the Research Institute, the Jewish Hospital of St. Louis, and the Department of Medicine, Washington U. School of Medicine.

introduction of hyaluronidase to enhance absorption from the connective tissues, and of fibrinolytic and nucleolytic enzymes as local enzymatic debriding agents, can be attributed in each case to a well founded developmental approach utilizing basic knowledge and employing appropriate quantitative and qualitative techniques to demonstrate the effects.

It was my great fortune to participate in the developmental work which led to the introduction of fibrinolysins and desoxyribonucleases, and the telling of that story will serve as a background for my future remarks.

The story behind the use of fibrinolysins goes back to 1933, when Dr. William S. Tillett made a very interesting observation. He was concerned with the effect of plasma on the agglutination of hemolytic streptococci, and traced this agglutinating phenomenon to the fibrinogen fraction of plasma.[2] Tillett then postulated that if plasma were incubated with a culture of hemolytic streptococci, the agglutination of the organisms might remove sufficient fibrinogen to prevent the plasma from subsequent clotting. His results were totally unexpected; the plasma in the presence of the culture of hemolytic streptococci clotted in a perfectly normal fashion but then the clot, surprisingly, rapidly dissolved. Tillett then demonstrated that there was a clot lysing principle in streptococcal culture filtrates,[3] apparently produced as a product of the organism's metabolism. He termed the substance, streptococcal fibrinolysin since it was quite obvious that the lysis of the plasma clots was occurring as a result of the enzymatic dissolution of fibrin. In 1940, Milstone working in Tillett's laboratory, made another interesting observation.[4] Milstone demonstrated that streptococcal fibrinolysin alone was incapable of dissolving fibrin but required the presence of a human serum globulin for fibrinolysis to proceed.

Shortly after Milstone's observation, Christensen,[5] working first with Tillett and then with McLeod, elucidated a tenable hypothesis of the workings of this fibrinolytic enzyme system (Fig. 1). Christensen pointed out that Milstone's serum globulin was in reality a naturally occurring inactive precursor of a proteolytic enzyme capable of digesting fibrin. This inactive precursor, termed plasminogen or profibrinolysin, was slowly spontaneously converted to the active enzyme, termed plasmin or fibrinolysin. Chloroform could be shown to accelerate the appearance of plasmin by removing inhibitors, but streptococcal fibrinolysin was unique in its ability to convert plasminogen to plasmin at a very rapid rate. Because of the enzymatic nature

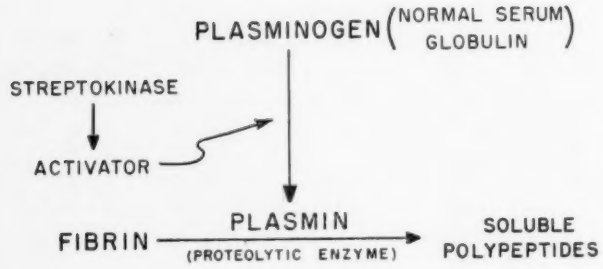


Fig. 1.—Schematic representation of fibrinolytic enzyme system of plasma. (Reprinted from Sherry, et al., Trans. Ass. Amer. Physicians 52: 288, 1957)

of the activation of plasminogen by streptococcal fibrinolysin, the latter was felt to be an activator or a kinase and was renamed streptokinase. Christensen in elucidating the components of this serum fibrinolytic enzyme system, had been forced into purifying streptokinase. By 1946, material was made available to Tillett and myself for clinical observation.

The pleural space was selected as the area for study of the effects of streptokinase injections since it was ideally suited for studies of this type. Undesirable accumulations of fibrin were commonplace in the pleural space, large samples of fluid for analysis could be obtained easily, and roentgenographic evidence of effects could be demonstrated. It was found that intrapleural injections of streptokinase in man were irritating but did not produce serious toxicity nor injury to living tissues. After a long period of preliminary study designed to determine the amount of streptokinase required to activate plasminogen in vivo, the therapeutic range was entered, i.e., injecting amounts of streptokinase which would consistently set into motion an active fibrin dissolving system. Then things began to happen, and there was no problem in demonstrating that clotted blood in the pleural space could be liquefied by local injections of streptokinase.[6]

Figure 2 illustrates observations on the very first patient in whom an attempt was made to dissolve a loculated coagulum in the chest. Shown in Figure 2 are the x-rays of a 21 year old male who had undergone a left pneumonectomy. Postoperatively, as shown on the left of Figure 2, a large multiloculated coagulum accumulated

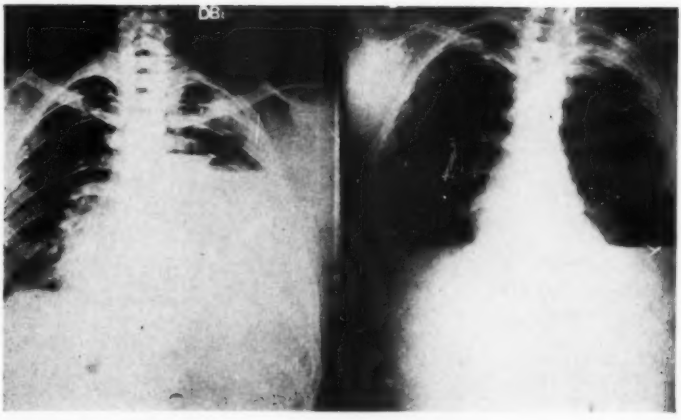


Fig. 2.—Effect of streptokinase in a case of loculated hemothorax. See text for details. (Reprinted from Tillett, W. S., and Sherry, S. J. Clin. Invest. 28:173, 1949)

in the left pleural space. During the postoperative course the patient became febrile, and infection of the pleural space was suspected. Because of the multiple loculations, repeated aspirations of the chest yielded only small amounts of sterile serosanguineous fluid. The febrile course persisted despite antibiotic therapy and it was deemed advisable to lyse the coagulum to determine whether there were hidden areas of infection. Streptokinase was injected into one of the loculated areas. The next morning fluoroscopy revealed a striking disappearance of all the loculations and complete liquefaction of the contents of the pleural space. Thoracentesis yielded 1300 cc of thin, sterile fluid following which the x-ray, shown on the right of Figure 2, was taken. Subsequent to the thoracentesis, the patient's febrile course spontaneously subsided. This case was dramatic indeed, and it was apparent that rapid lysis of fibrin could be accomplished enzymatically for therapeutic purposes in man.

When streptokinase was injected into the chest of patients with thick purulent empyemas, it was noted that a dramatic thinning of the purulent exudate occurred. There was good reason, along biochemical lines, to suspect that the physical characteristics of thick viscous pus were not due to fibrin but to some other constituent present in large amounts in the sediment of the exudate. Thus the rapid lysis of the thick exudate by the streptokinase preparation sug-

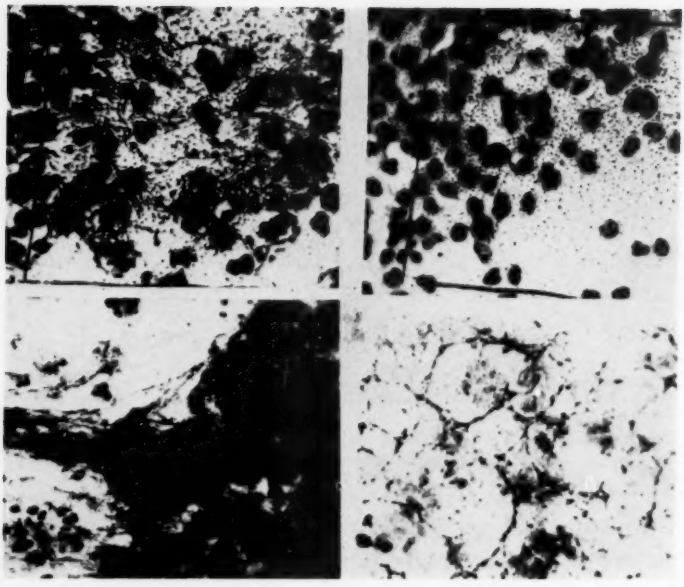


Fig. 3.—Feulgen stains of purulent exudates derived from patients with pleural empyemas. See text.

gested the presence of another streptococcal enzyme. In 1948, the major constitutent of the solid sediment of purulent exudates was identified as desoxyribonucleoprotein, a viscous, stringy, insoluble protein derived from the nuclei of cells undergoing degeneration in areas of exudation and suppuration.[7] The streptococcal enzyme present in our streptokinase preparation and capable of causing the rapid breakdown of this nucleoprotein proved to be a desoxyribonuclease.[8] For convenience, it was termed streptodornase.

When the Feulgen stain, which is specific for DNA protein, was applied to the smears of exudates, the presence and distribution of this nucleoprotein could be readily demonstrated. Shown in Figure 3 are four exudates stained by the Feulgen method. The nucleoprotein is dark staining material and appears in the nuclei of the living and dead cells, and scattered extracellularly. The top two smears in Figure 3 are from acute empyemas. It will be noted that the extracellular nucleoprotein appears as granules and short fibrous strands. The lower two smears in Figure 3 are from chronic tubercu-

lous empyemas, and here, the nucleoprotein has polymerized into an extensive extracellular network.

The streptodornase in our preparations acted in a dramatic fashion in vivo as well as in vitro. The smear shown on the left of Figure 4 is a Feulgen stain of the pus aspirated from a suppurative tuberculous node in a young child. The node was then injected with the streptococcal enzyme concentrate. Twenty minutes later, thin purulent fluid was aspirated and the smear, shown on the right of Figure 4, was made. Only the nuclei of intact cells remain. Detailed studies by Johnson revealed that the streptococcal enzymes did not affect living cells but rapidly dissolved the nucleus of degenerating and dead cells, as well as all extracellular DNA protein.

As might be expected, the gross effect on thick pus was very striking. The tube, shown on the left of Figure 5, contains a sample of purulent fluid removed from the chest of a patient with a thick tuberculous empyema, just prior to the intrapleural instillation of the streptococcal enzyme preparation. The tube on the right of Figure 5 contains a sample of exudate removed one hour after the injection, and demonstrates that the heterogeneous nature of the sediment has been broken up into homogeneous layers, and the major portion of the sediment dissolved.

The ability of the streptococcal enzyme preparation to incite the lysis of the two major insoluble constituents found in areas of infection, namely, fibrin and DNA protein led to the concept of an enzymatic debridement and the use of this concept was extended to localized disease in various areas of the body.[9] The effects which could be attributed to the local application of these streptococcal enzymes are summarized as follows:

RESULTS OF ENZYMATIC DEBRIDEMENT WITH SK-SD

1. Cleansing of area and surface of infection of fibrin and desoxyribonucleoprotein (DNP).

2. Facilitates drainage of areas of loculated purulent, sanguineous, and fibrinous accumulations.

3. Liberation of hidden bacteria with exposure to:
   a) antimicrobial agents
   b) immune forces

4. Stimulation of tissues with resultant increased growth potential.

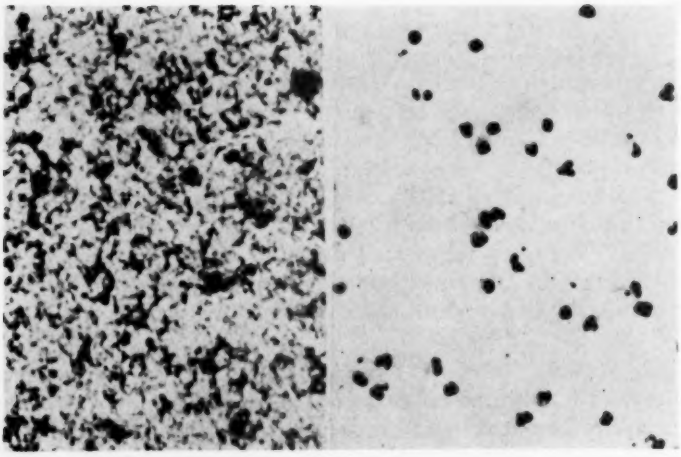


Fig. 4.—In vivo effect of streptodornase on desoxyribonucleoprotein of purulent exudate (Feulgen stain).

In the patient studies which followed, detailed attention was given to elaborating the principles involved in the use of these enzymes, correlating in vitro with in vivo observations, and making appropriate quantitative measurements rather than relying on empirical clinical appraisal. In addition, fundamental problems raised by the in vivo studies, such as the effect of the enzymes on living and dead cells, the extent of the degradation of fibrin and DNA by these enzymes, and the development of new techniques for assaying the enzymes in biological fluids, were taken into the laboratory and studied in great detail.

Out of this work emerged a rational approach to the use of enzymes in a variety of disease states. The use of streptokinase-streptodornase proved effective in many patients whilst in others the results were disappointing. In each case where the results were disappointing, the lack of effect could usually be shown to be due to an aberration of one of the principles involved in their use, or a lack of understanding of how to use these enzymes in relation to a more complex disease problem. For example, it became apparent that additional enzymes would have to be developed for use in areas where there were large accumulations of respiratory mucin, or ex-

tensive skin and connective tissue sloughs, since these involved substrates not susceptible to the action of the streptococcal enzymes. Also, it had to be stressed that the enzymes were developed primarily as an adjunct to the management of various disease states and were not designed to replace any of the other basic principles involved in the management of disease.

However, as a consequence of these studies, the broad aspect of local enzyme therapy by agents capable of depolymerizing highly viscous substances or fibrous proteins is now well established. Proper exploitation of this relatively new field of therapy still requires a considerable number of further developments, the more important of which include: 1) the development of better methods for getting enzymes into direct and sustained contact with the substrate; 2) the development of techniques or procedures by which the irritating qualities of some of the enzymes in current use can be minimized, particularly when they are used in small, fixed spaces; 3) the identification of substrates, other than those presently recognized, which may contribute significantly to disease, or impair normal healing processes; and 4) the identification and development of new enzymes which are capable of lysing known substrates which contribute to the maintenance of disease.

Let us consider a logical extension of this earlier work with fibrinolysins and nucleases, namely, the development of enzyme therapy for systemic use. By the latter, one refers to the systemic injection of enzymes in high enough concentration, and for long enough periods of time, to enzymatically degrade specifically defined materials which have accumulated in an undesirable fashion either in the blood vessels themselves, or in adjacent areas into which the enzyme may diffuse. As an illustration, let us consider the possibility of producing controlled fibrinolysis in vivo for the therapy of thromboembolic disease. The magnitude of the benefits of such a procedure, if it could be successfully developed, is readily apparent, since thrombo-embolic disease represents a major cause of morbidity in man, today.

Considerable progress already has been made in this direction, and I should like to tell you about our own studies which have been carried out in association with Drs. Anthony Fletcher and Norma Alkjaersig. It should be recognized that somewhat similar studies are in progress in several other institutions in this country, particularly by groups under the direction of Tillett, Cliffton, Ambrus and von

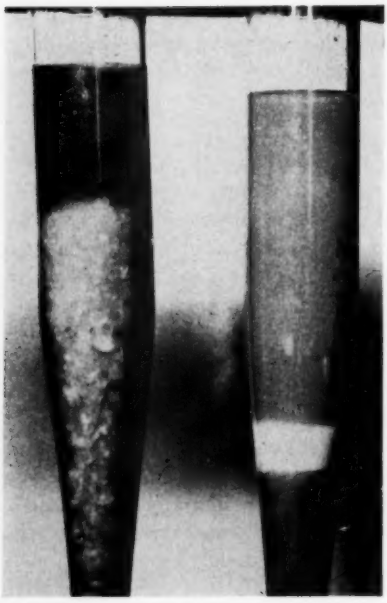


Fig. 5.—Rapid lysis by streptococcal concentrate of purulent pleural exudate within pleural cavity of patient. (Reprinted from Tillett, W. S., and Sherry, S. J. Clin. Invest. 28:173, 1959)

Kaulla. Although our individual approaches may differ, and different enzymes be employed, the ultimate objectives are the same.

In experimental animals considerable success in producing intravascular fibrinolysis can be achieved with intravenous injections or infusions of streptokinase. Thus Johnson and Tillett[10] were able to dissolve preformed venous thrombi in rabbit ear veins by intravenous infusions of streptokinase. We have demonstrated that intravenous injections or streptokinase into dogs may result in the dissolution of experimental femoral artery thromboses.[11] An example is illustrated in Figure 6. Shown on the left of Figure 6 is an experimental thrombus observed in the femoral artery of a control animal, five days after its production. The artery is cut in a semi-longitudinal fashion and evidences of early organization of the well formed thrombus is evident. The section of artery, shown on the right of Figure 6 was taken from a streptokinase treated animal at the same time as the

Fig. 6.—Dissolution by streptokinase treatment of an experimental thrombus in the femoral artery of a dog.

specimen from the control animal. The lumen is patent with only a few shreds of clot present.

In addition to the ability of systemically injected streptokinase to incite the dissolution of intravascular thrombi, evidence has been obtained suggesting that extravascular deposits of fibrinous exudate can be lysed by intravenously administered streptokinase.[12] These experiments are of considerable importance from a fundamental standpoint since they indicate that the concept of systemic specific enzyme therapy is not limited to the vascular tree but may be extended to involve extravascular areas into which the enzyme may diffuse. In these experiments a traumatic fibrinous peritonitis which could be expected to proceed to organization was produced in dogs by scarifying an area of peritoneal wall with a vegetable grater. The animals

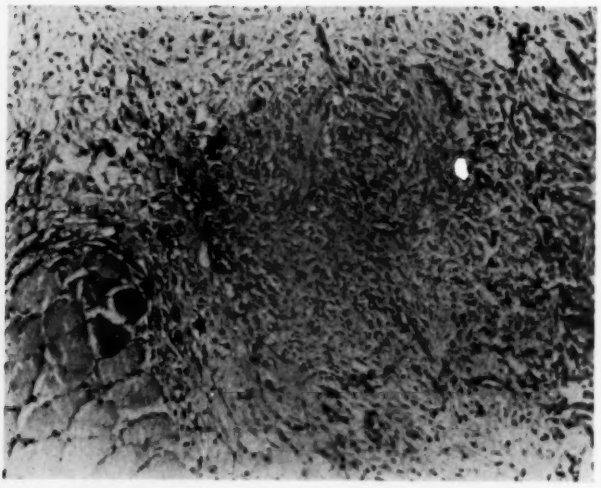


Fig. 7.—Effect of intravenous streptokinase on experimental traumatic peritonitis in the dog (control animal). (Reprinted from Sherry, et al. Proc. Soc. Exptl. Biol. and Med. 90:1, 1955)

were sacrificed on the twelfth day and the abraded area examined grossly and histologically. As anticipated, almost every one of the control animals, developed dense adhesions at the site of previous trauma. In contrast, only an occasional animal, receiving large amounts of streptokinase intravenously for a three day period after the abrasive injury, developed any adhesions.

Figure 7 demonstrates the extent of the exudate seen on the fifth postoperative day in one of the control animals. The rectus muscle is seen at the lower left and the extensive fibrinous exudate infiltrated with cellular elements extends to the top of the figure. Early organization is under way, extending down between the muscle bundles. Figure 8 demonstrates the scanty exudate seen in a streptokinase treated animal, also taken on the fifth postoperative day, for comparison to the control. Organization is not evident and it is improbable that adhesions would have developed in this animal.

Following the demonstration that clot lysis could be produced in vivo, in animals, by fibrinolytic means, studies with intravenous streptokinase in man were instituted. Although the progress of this

work was impeded initially by a high incidence of undesirable pyrogenic reactions, it could be demonstrated that plasminogen could be activated in the circulation with no unusual toxicity or hazard to the patient.[13]

Although, all the emphasis in the developmental work in man by other groups is on maintaining high levels of circulating fibrinolysin, our approach to intravascular fibrinolysis has differed since it is based on an investigation of the mechanism by which experimental clots are actually dissolved. The results of this in vitro study indicate that the concentration of activator in the circulation is more critical in effecting clot lysis than the level of fibrinolysin or plasmin itself.[14] Consideration was given, as shown in Figure 9, to two alternative schemes by which intravascular clot lysis may occur. First, clot lysis may result from the direct action of circulating plasmin. With this mechanism, the concentration of plasmin or fibrinolysin in the circulation is the critical factor in determining the rate of fibrinolysis. Alternatively, since all human thrombi contain considerable amounts of intrinsic plasminogen as a consequence of the adsorption of this substance during the process of clotting, clot lysis may result from the diffusion of activator into the clot. Under this latter scheme, the concentration of circulating activator is the critical factor.

To decide this choice, we measured the rate of fibrinolysis by the amount of radioactivity released from preformed I^{131} trace labelled human plasma clots. These clots were incubated in solutions containing either human plasmin alone, activators alone, or mixtures of plasmin and activator. The proteolytic activity of the test solutions were measured by a standard casein method. The results of these experiments, one of which is illustrated in Figure 10, demonstrate that clots incubated in the presence of activators undergo rapid fibrinolysis, whereas clots incubated in the presence of the proteolytic enzyme plasmin alone are poorly digested.

In Figure 10 the data are presented in three panels; on the left, are shown the effects of a purified preparation of human plasmin alone; in the center, the effects of streptokinase alone; and on the right, the results obtained with a mixture of streptokinase plus plasmin. The broken line refers to radioactivity released from the tagged plasma clots, while the solid line refers to the proteolytic activity of the substance under investigation. The data in each panel are plotted as a function of the concentration of the substance under study. It will be noted on the left of Figure 10 that plasmin, at very significant levels of proteolytic activity, produces very little lysis of

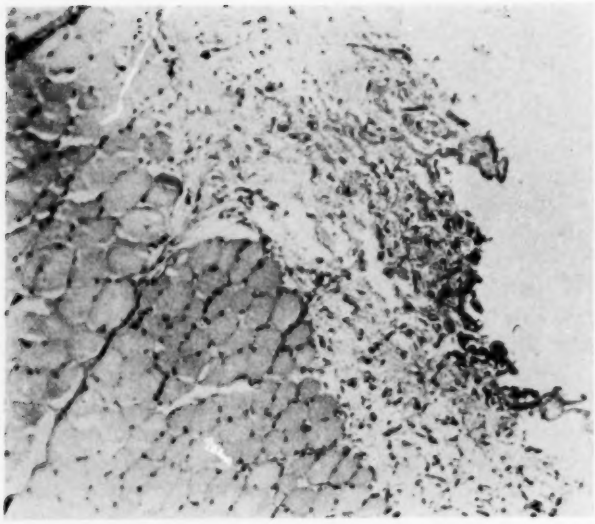


Fig. 8.—Effect of intravenous streptokinase on experimental traumatic peritonitis in the dog (treated animal). (Reprinted from Sherry, et al. Proc. Soc. Exptl. Biol. and Med. 90:1, 1955)

the tagged clots. In sharp contrast, as seen in the center, streptokinase, with no proteolytic activity, produces marked clot lysis, an effect directly related to the streptokinase concentration. On the right of Figure 10, it will be noted that the addition of streptokinase to the previously ineffective plasmin preparation does not increase the proteolytic activity of the mixture but results in a powerful clot lysing preparation. From these, and similar experiments utilizing other activators, as well as other techniques, we have concluded that the fibrin lysing power of plasma upon thrombi is dependent upon its activator content, and relatively independent of its proteolytic activity or plasmin content.

Accordingly, in patients, we have deemed it desirable to induce and then maintain high levels of circulating activator rather than high levels of circulating fibrinolysin. This has been made possible by the recent availability of highly purified streptokinase preparations which are well tolerated in patients. Treatment has been instituted by the intravenous injection of a priming dose of streptokinase, dependent in amount on the level of circulating antibody, and vary-

ing between 10,000 and 200,000 units. Thereafter, the level of activator has been maintained by the intravenous administration of 50 to 100,000 units of streptokinase an hour during the treatment period. This regime, designed as a consequent of patient studies with isotopically labelled streptokinase, maintains a plasma level of 3 to 10 streptokinase units/ml.

Figure 11 illustrates the biochemical changes induced on the second day of treatment in an 84 year old man suffering from a femoral artery thrombosis. The patient received three streptokinase injections of 200,000 units each at two hourly intervals and observations were made over a 16 hour period. The top graph of Figure 11 describes the plasminogen and fibrinogen levels. Immediately beneath the top graph are observations on the lysis time of spontaneously clotting whole blood specimens. This test is a crude measure of circulating plasmin. In the lower graph are shown observations on the ability of the patient's plasma to produce zones of lysis on a fibrin plate test, and to lyse radioactive human plasma clots.

It will be noted that the fibrinogen levels were not significantly altered during the entire period of observation. Immediately following the first streptokinase injection, the plasminogen concentration fell to insignificant levels, as a consequence of its rapid activation, and remained depressed during the period of repeated injections. At the end of the period of observation, the plasminogen concentration had returned to a high level. None of the spontaneously clotted whole blood specimens lysed over a 24 hour period, and this observation, together with other determinations, showed a virtual absence of plasmin in the circulation. The rapid disappearance of plasmin from the circulation is attributed to the powerful inhibitory action of the blood. In contrast, as shown in the lower graph, the streptokinase injections were associated with a striking rise in the clot lysing activity of the plasma, which was maintained during the period of SK injections but returned to the pretreatment range by the end of the period of observation. These data illustrate in an unequivocal fashion the dissociation of the fibrin lysing power of the plasma from its plasmin content.

At present more than 50 patients with thrombo-embolic disorders have been treated with very large doses of streptokinase, i.e., a million units or more. These include patients with acute coronary thrombosis and myocardial infarction; cerebral vascular thrombosis; peripheral arterial thrombosis; retinal artery thrombosis; deep vein thrombophlebitis, with or without complicating pulminary emboli; slowly

ALTERNATIVE SCHEMES OF CLOT LYSIS

MECHANISM OF CLOT LYSIS	CRITICAL FACTOR
1. LYSIS OF CLOT BY CIRCULATING PLASMIN	PLASMIN CONC.
2. DIFFUSION OF CIRCULATING ACTIVATOR INTO CLOT ↓ ACTIVATION OF INTRINSIC CLOT PLASMINOGEN ↓ CLOT LYSIS	ACTIVATOR CONC.

Figure 9

resolving lobar pneumonia; and penetrating wounds or infections of the eye. These diseases although of diverse etiology and clinical symptomatology all have the common feature of fibrin clots or fibrin exudates.

Although any attempt to clinically evaluate this form of therapy at the present time would be premature, we have obtained evidence, in a number of instances, which suggests that in vivo fibrinolysis has been produced. The course in two patients, one with pulmonary emboli secondary to thrombophlebitis, and the other with a fibrinous exudate in the anterior chamber of the eye have been selected for illustration.[14]

REPORT OF CASES

CASE 1. R.B., a 61 year old farmer, noted pain and tenderness in the left calf, three weeks prior to admission. For the entire two week period before hospitalization, the patient was incapacitated by severe dyspnea or minor exertion. Two days before admission, he experienced pain in the left inguinal region followed by tense edema of the entire left leg. On admission to Barnes Hospital, the left thigh and calf measured 3 cm greater than the right. Chest x-ray and electrocardiogram, shown on the left of Figure 12, revealed cardiomegaly and right bundle branch block, presumably as a result of multiple pulmonary emboli. The patient was treated over a four day period with a total of 1.7 millions units of streptokinase. Repeat

chest x-ray and electrocardiogram taken shortly after the completion of the streptokinase therapy, as shown on the right of Figure 12, revealed a normal heart size and a disappearance of the right bundle branch block. The phlebitis had completely subsided. On subsequent mobilization there was no evidence of diminished cardiac reserve or of postphlebitic edema.

CASE 2. The second patient was of particular interest since it is well recognized that fibrin in the anterior chamber of the eye does not spontaneously resolve. M.S., a 71 year old man, developed signs of an intraocular infection three days following the removal of a cataract. Culture of the anterior chamber fluid revealed a diplococcus. During intensive antibiotic therapy, a dense fibrinous exudate formed in the anterior chamber. He was given 1 million units of streptokinase intravenously over the next four days. By the third day of treatment, slip lamp examination suggested resolution of the fibrinous exudate. On the fourth day, marked clearing of the anterior chamber was evident and over the next two days all traces of the fibrinous exudate disappeared.

COMMENT

As a result of these studies we now know that high levels of fibrinolytic activity can be sustained in the circulation of patients for long periods of time without any undue hazard. We have noted some minor bleeding, particularly from the sites of operative wounds, but we have not, as yet, seen any severe bleeding. Although we are very encouraged with the development of these patient studies, we recognize that assessing the value of this procedure in disease states will be extremely difficult because of the real part that bias may play. As a result these studies have been restricted to one disease, namely, acute coronary thrombosis, and are being conducted by means of a double blind study. Only by means of this type of study, where neither the patient, nor those evaluating the study, know which agent has been used, can the element of bias be eliminated.

If these studies should prove successful, fibrinolytic therapy can be applied to any number of diseases where undesirable accumulations of fibrin occur. Besides the diseases mentioned, it should prove very useful in the treatment of subacute bacterial endocarditis or in almost any type of deep seated inflammatory or infectious disease occurring in any area of the body. The possible scope of fibrinolytic therapy is enormous not only for the treatment of disease but perhaps for prophylaxis as well.

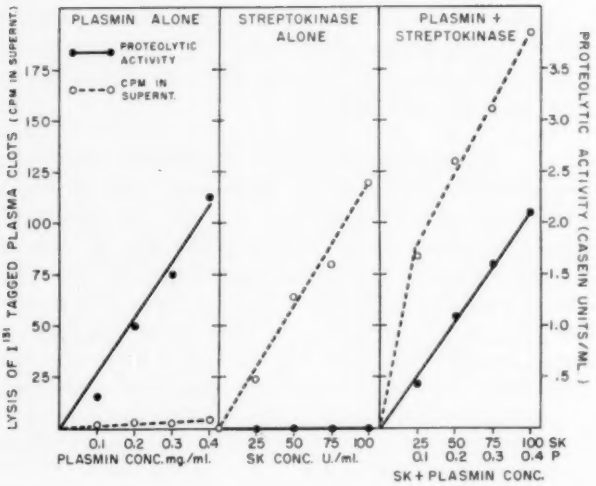


Fig. 10.—Effect of plasmin and streptokinase on I^{131} tagged human plasma clots. (Reprinted from Sherry, et al. Trans. Ass. Amer. Physicians 70:288, 1957)

Of course, there is no reason to believe that streptokinase will prove to be the only or best agent for producing controlled fibrinolysis in patients. Other activators, e.g., urokinase, which can be derived from animal or human urine, may prove to be less antigenic, and more useful for patient therapy. It is interesting to note that Ploug[15] in Denmark recently has reported on relatively simple purification procedures for urokinase which have resulted in a several thousand-fold concentration and purification of this substance. It is also possible that purified preparations of human fibrinolysin derived from human plasma can successfully be developed for system fibrinolytic therapy.[16,17] However, if our own views are correct, the use of activators of enzymes wherever possible may prove to be a more promising approach to enzyme therapy, than the use of enzymes themselves.

At present, the development of systemic therapy with specific enzymes is not restricted to studies on fibrinolysins. Tillett and his group recently have reported on the use of intravenous pancreatic desoxyribonuclease for the therapy of lung abscesses.[18] In this latter disease, one of the major therapeutic problems is to improve drainage

of the thick purulent exudate which accumulates in the abscess cavity. If the exudate can be thinned, better drainage through the natural respiratory passages may be expected, and spontaneous healing may then occur. Tillett and his group now believe that they can achieve better contact between enzyme and substrate through systemic administration of the desoxyribonuclease rather than by bronchoscopic instillation or aerosols. Pancreatic desoxyribonuclease can be given intravenously in large amounts without systemic reaction, and the clinical results have been encouraging.

If these studies to which I have referred should prove successful, then the concept of systemic therapy with enzymes will be firmly established, and the usefulness of this type of enzyme therapy will be considerably extended. In considering systemic enzyme therapy, one should not limit his thinking to fibrin and DNA protein. There are a number of other undesirable materials which accumulate in disease states, and contribute significantly to the morbidity of the illness. Theoretically, these substances could be removed by enzymatic means. For example, there are a large group of diseases in which symptomatology is related to the deposition of abnormal materials in the walls of blood vessels and in the connective tissues throughout the body. Under this group we may include rheumatoid arthritis, systemic lupus erythematosus, scleroderma, polyarteritis, dermatomyositis, amyloidosis, paraamyloidosis, Kimmelstiel-Wilson's disease, and a number of others. In some of these diseases the fibrinoid-like material needs further identification while in others information is available about the composition of the abnormal deposits. Why can we not rid the body of these materials by specific systemic enzyme therapy? Along similar lines, can we develop lipases for the therapy of fat emboli, or other enzymes for the treatment of amniotic fluid emboli? All of these diseases offer a practical challenge to the therapeutic enzymology of the near future.

Let us also consider a number of diseases, as illustrated by gout, in which sparingly soluble yet relatively simple compounds accumulate in the body and produce disease by precipitating out in joints, connective tissues, and kidney. Why can't their therapy be more aggressively managed by the use of appropriate enzymes?

Although our discussion has been limited to enzymatic therapy aimed at ridding the body of well defined deposits of insoluble materials occurring either locally or in the extracellular and vascular compartments of the body, this viewpoint certainly need not be so restrictive. Undesirable, yet soluble constituents can also be brought under enzymatic attack. As an example, we may note the recent

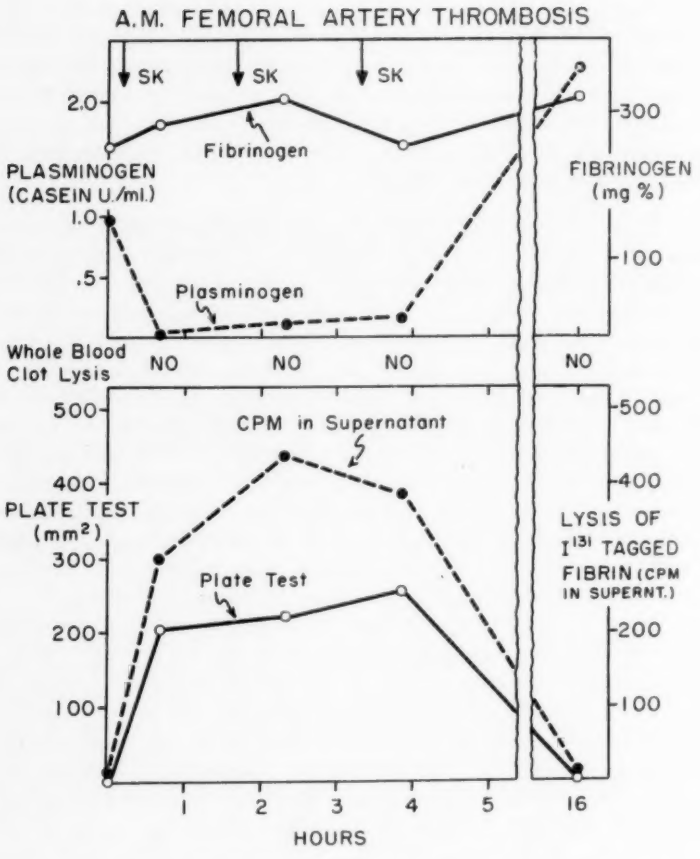


Fig. 11.—Biochemical change induced by intravenous streptokinase in a patient with a femoral artery thrombosis. (Reprinted from Sherry, et al. Trans. Ass. Amer. Physicians 70:288, 1957)

introduction of intramuscular penicillinase injections for the treatment of hypersensitivity reactions to penicillin.[19] By markedly reducing the concentration of the residual penicillin in the circulation and connective tissue depots, as a consequence of penicillinase injections, investigators at the Great Lakes Naval Hospital believe they have obtained results which are superior to other methods of treatment for the annoying and sometimes serious reactions to penicillin. This

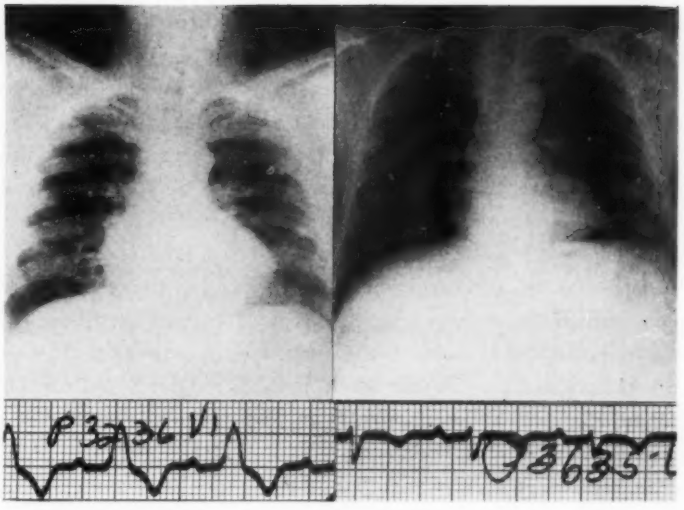


Fig. 12.—Effect of intravenous streptokinase on a patient with multiple pulmonary emboli secondary to thrombophlebitis. (Reprinted from Sherry, et al. Trans. Ass. Amer. Physicians 70:288, 1957)

is an exceedingly interesting approach and makes one wonder whether a similar approach can be developed for other sensitivity reactions as well as other types of diseases.

Another area which is worthy of further exploration and could be studied at the present time, relates to enzymatically altering the normal state on a systemic basis. All of us are aware of the local influences of hyaluronidase on altering the diffusion characteristics of the connective tissue. Could we utilize this effect on a systemic basis to favorably alter the course of certain diseases? For example, could we enhance the mobilization of fluid in cardiac failure by combining systemic hyaluronidase injections with appropriate diuretic therapy?

In all these remarks, consideration has been given only to materials or substances which are in the vascular or connective tissue compartments of the body since these may readily come under attack

in the foreseeable future. We have not considered the possibility of the use of enzymes for intracellular purposes since there is very little evidence that enzymes administered exogeneously can penetrate the peculiar permeability characteristics of the cellular compartment. If methods can be developed for allowing exogeneously administered enzymes to penetrate the intracellular compartment, then the clinical potentiality of enzyme therapy will become enormously magnified. As you probably all appreciate, the contributions of biochemistry to medicine in recent years have far outstripped those of pathology and physiology. Knowledge is rapidly expanding concerning the metabolic blocks, abnormal biochemical shunts, and enzyme deficiencies which are pathogenetically involved in various disease states but particularly those with a constitutional or genetic background. It is certainly conceivable that when methods are developed for delivering appropriate enzymes to the intracellular compartment that the biochemical lesion underlying a variety of diseases can be repaired and a more normal state of metabolism restored. In selected situations the validity of this concept has been amply demonstrated by the dramatic results obtained through the use of specific coenzymes which have no difficulty in traversing cell membranes. The potentialities of this type of enzyme therapy, i.e., to restore normal metabolism is so great that it would encompass the entire field of medicine but at this time remains beyond our reach.

The intent of this presentation has been a rather broad and provocative look ahead at what might be considered possible to accomplish therapeutically with enzymes, based upon existing biochemical and medical research knowledge. It is my belief that the future of enzyme therapy is a bright one, indeed, with relatively unlimited horizons. However progress in this field of therapeutics, like all other areas of medical science, must depend initially on two things: the key discoveries of those involved in basic investigation; and close collaboration between the laboratory investigator and the clinical investigator.

JEWISH HOSPITAL

REFERENCES

1. Morris, R. T.: The Action of Trypsin, Pancreatic Extract, and Pepsin upon Sloughs, Coagula, and Muco-Pus. N. Y. Med. J. 53:424, 1891.

2. Tillett, W. S., and Garner, R. L.: The Agglutination of Hemolytic Streptococci by Plasma and Fibrinogen. Bull. Johns Hopkins Hosp. 54:145, 1934.

3. Tillett, W. S., and Garner, R. L.: The Fibrinolytic Activity of Hemolytic Streptococci. J. Exptl. Med. 58:485, 1933.

4. Milstone, H.: A Factor in Normal Human Blood Which Participates in Streptococcal Fibrinolysis. J. Immunol. 42:109, 1941.

5. Christensen, L. R.: Streptococcal Fibrinolysis: A Proteolytic Reaction Due to a Serum Enzyme Activated by Streptococcal Fibrinolysin. J. Gen. Physiol. 28: 363, 1945.

6. Tillett, W. S., and Sherry, S.: The Effect in Patients of Streptococcal Fibrinolysin (Streptokinase) and Streptococcal Desoxyribonuclease on Fibrinous, Purulent, and Sanguinous Pleural Exudations. J. Clin. Invest. 28:173, 1949.

7. Sherry, S., Tillett, W. S., and Christensen, L. R.: Presence and Significance of Desoxyribose Nucleoprotein in the Purulent Pleural Exudations of Patients. Proc. Soc. Exper. Biol. and Med. 68:179, 1948.

8. Tillett, W. S., Sherry, S., and Christensen, L. R.: Streptococcal Desoxyribonuclease: Significance in Lysis of Purulent Exudates and Production by Strains of Hemolytic Streptococci. Proc. Soc. Exper. Biol. and Med. 68:184, 1948.

9. Tillett, W. S., and Sherry, S., Christensen, L. R., Johnson, A. J., and Hazelhurst, G.: Streptococcal Enzymatic Debridement. Ann. Surg. 131:12, 1950.

10. Johnson, A. J., and Tillett, W. S.: The Lysis in Rabbits of Intravascular Blood Clots by the Streptococcal Fibrinolytic System (Streptokinase). J. Exptl. Med. 95:449, 1952.

11. Sherry, S., Titchener, L., Gottesman, P., Wasserman, P., and Troll, W.: The Enzymatic Dissolution of Experimental Arterial Thrombi in the Dog by Trypsin, Chymotrypsin, and Plasminogen Activators. J. Clin. Invest. 33:1303, 1954.

12. Sherry, S., Callaway, D. W., and Freiberg, R.: Prevention of Postoperative Adhesions in the Dog by Intravenous Injections of Plasminogen Activators. Proc. Soc. Exptl. Biol. and Med. 90:1, 1955.

13. Tillett, W. S., Johnson, A. J., and McCarty, W. R.: The Intravenous Infusion of the Streptococcal Fibrinolytic Principle (Streptokinase) into Patients. J. Clin. Invest. 34:169, 1955.

14. Sherry, S., Fletcher, A. P., Alkjaersig, N., and Smyrniotis, F. E.: An Approach to Intravascular Fibrinolysis in Man. Trans. Assoc. Amer. Physicians 52:288, 1957.

15. Ploug, J., and Kjeldgaard, N. O.: Isolation of a Plasminogen Activator (Urokinase) from Urine. Arch. Biochem. Biophys. 62:500, 1956.

16. Cliffton, E. E.: The Use of Plasmin in Patients. Ann. N. Y. Acad. of Sciences 68:209, 1957.

17. Ambrus, J. L., Ambrus, C. M., Back, N., Sokal, J. E., and Collins, G. L.: Clinical and Experimental Studies on Fibrinolytic Enzymes. Ann. N. Y. Acad. of Sciences 68:97, 1957.

18. Ayvazian, J. H., Johnson, A. J., and Tillett, W. S.: The Use of Parenterally Administered Pancreatic Desoxyribonuclease as an Adjunct in the Treatment of Pulmonary Abscesses. Am. Rev. Tuberc. 76:1, 1957.

19. Minno, A. M., and Davis, G. M.: Penicillinase in the Treatment of Penicillin Reactions. J. Am. M. Ass. 165:222, 1957.

III

EPIDERMOID CHOLESTEATOMA AND CHOLESTEROL GRANULOMA

EXPERIMENTAL AND HUMAN

I. FRIEDMANN

LONDON, ENGLAND

In 1829 Cruveilhier[7] described the "pearly tumor" which the famous anatomist Johannes Müller first called "cholesteatoma" in 1838.[17] Subsequently and particularly since the development of modern otology the questions of pathogenesis, terminology and the problematic etiological association with cholesterol of the "cholesteatoma" of the ear have been a matter for much argument and discussion. The extent of topical interest in these problems was amply indicated in a recent discussion on "Cholesteatosis of the Attic" in the Otological section of the Royal Society of Medicine (1958).

Rüedi[19] in his opening paper at this symposium reviewed the present state of knowledge of this condition and furnished additional experimental proof of the validity of the immigration theory; Tumarkin[27] and Birrell,[3] on the other hand, have focused their attention on terminological reform.

It is proposed here to reconsider the histogenesis and nomenclature of epidermoid cholesteatoma and the related condition of cholesterol granuloma in the light of some recent experimental work.

The terms "epidermoid cholesteatoma" and "cholesterol granuloma" have been applied in previous reports of this systematic analysis of the pathology of otitis media[8-11] and will be further discussed.

EPIDERMOID CHOLESTEATOMA

Structure. The epidermoid cholesteatoma is a cystic structure lined by keratinizing stratified squamous epithelium resting on fibrous

---

From the Department of Pathology, The Institute of Laryngology and Otology, London.

Presented in the discussion on "Cholesteatosis of the Attic," Otology Section, Royal Society of Medicine, February 7, 1958.

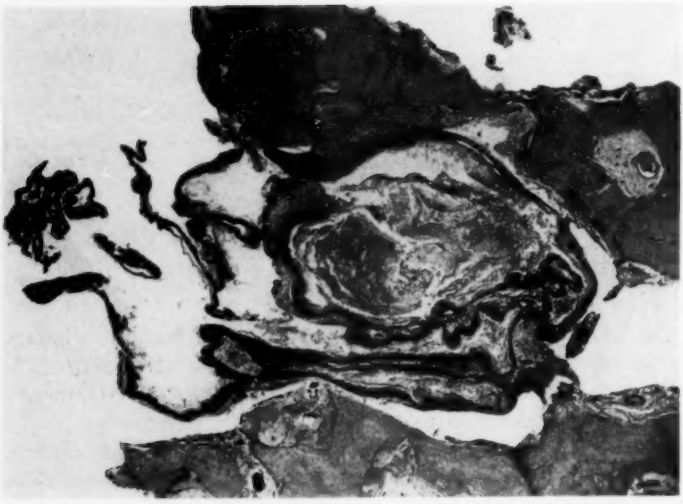


Fig. 1.—Epidermoid Cholesteatoma. Note bag-like structure completely removed at mastoidectomy operation. The squamous epithelial lining appears to form a stalk and there is an opening leading into the cavity proper. (G 908) X 25.

stroma of variable thickness, which may contain some elements of the original mucous lining. The keratinized layers of the epithelium are innermost and are desquamated into the cavity of the cyst and form its contents, often with a generous admixture of pus (Fig. 1). It must be stressed that the epidermoid cholesteatoma is an epithelial product of keratinizing stratified squamous epithelium showing hyperkeratosis.

Histogenesis. The following theories have been advanced to explain the origin of the squamous epithelium in the middle ear cleft: the congenital, the immigration, the implantation, the metaplasia and hyperplasia theories.

1. *Congenital Origin.* The congenital origin of some epidermoid cysts of the petrous bone is indisputable (Lancet, 1958). The meninges and a large part of the cranium are ectodermal in origin arising from the neural crest. J. S. Tytus and J. Pennybacker[28] have recorded 43 cases of keratinous epithelial cysts in and about the central nervous system. Their work illustrates the many different sites in

Fig. 2.—Section of bone fragment with cholesterol granuloma. Note large numbers of cholesterol clefts embedded in fibrous granulation tissue filling a mastoid cell. Hematoxylin and eosin X 60 I 1117

which these lesions may arise: two were pericranial, six orbital, six petrous, two diploic, two suprasellar, seven intracerebral, three cerebello-pontine, eight midline subtentorial and seven spinal. There were six petrous lesions which included cholesteatomas. Thus occasionally epidermoid cysts or cholesteatoma of the petrous bone may be formed in this way and may in turn become infected from the middle ear. This origin, however, accounts for only a small number of genuine cases of epidermoid cholesteatoma. Schroer[21] in common with other authors altogether disputes the validity of this theory, basing his opinion on earlier embryological work. Rüedi[19] has found no evidence of embryonic cell nests in 124 temporal bones sectioned.

The only epidermoid cholesteatoma in which such an origin had to be considered was seen in this hospital in a man 65 years of age, in whom a large dermoid cyst or epidermoid cholesteatoma had been removed from the posterior cranial fossa (Mr. Radley Smith). Six months later the cavity in the posterior fossa was again explored (Professor F. C. Ormerod) when the petrous bone was found almost entirely eroded away. Its remnants and most of the residual mastoid process including the styloid process were also removed. The possi-

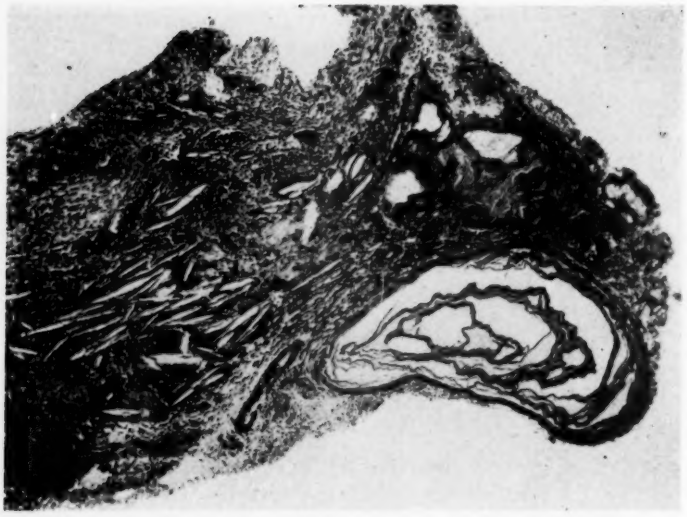


Fig. 3.—Epidermoid Cholesteatoma and Cholesterol Granuloma. This combination has been frequently observed. (I 103) X 75.

bility of an infectious origin for this cyst cannot, however, be entirely excluded as there was a history of homolateral facial palsy since 24 years of age.

2. *Immigration.* The immigration theory was advanced by Habermann[12] and was based upon the well-known pathological phenomenon of the epithelialization of sinus and fistula tracks. This postulated that cholesteatomata were produced by the ingrowth of keratinizing epidermis from the external auditory meatus through a perforation in the tympanic membrane into the tympanic cavity.

The theory has been challenged by the finding of cholesteatoma in patients with an apparently intact drumhead. In view of the clinical difficulty of assessing the histological integrity of the tympanic membrane this argument is obviously a dubious criticism.

Both human and experimental evidence strongly supports Habermann's theory.

3. *Implantation Cholesteatoma.* Squamous epithelium may be accidentally introduced into the middle ear following a fracture of

the temporal bone region.[21] Keratinizing squamous epithelium in ectopic sites seems to behave with uniformity irrespective of the site and originating mechanism. It rounds off into a cyst filled with keratinized matter forming in fact epidermoid cysts.

In this connection it is interesting to mention that intraspinal epidermoid or pearly tumors resembling cholesteatoma have been found in patients treated for tubercular meningitis, by Choremis and associates.[6] When streptomycin was introduced in the treatment of tuberculous meningitis, the C.S.F. was tapped by the authors usually for from three to five months. Therefore, it is probable that by the multiple punctures epithelial cells were implanted in the spinal canal. The process was extremely slow and the first symptoms appeared from three to seven years after the treatment of meningitis.

More recently, in the German literature, attention has been drawn to the development of "flap"-cholesteatoma (Lappen-cholesteatoma) as a late complication of tympanoplasty operations.[2] Here we are dealing with the same underlying phenomenon, i.e., the epidermis introduced by the surgeon may in some cases undergo hyperkeratosis and produce epidermoid cysts. This again has been noted in old mastoidectomy cavities where the term "inclusion dermoid" has been applied to similar structures.

4. *Metaplasia.* Squamous metaplasia has often been suggested as a possible explanation for the occurrence of squamous epithelium in the middle ear spaces. These are lined, normally, by flat endothelium-like cells resting on thin layers of connective tissue. In the course of chronic infections the epithelium assumes the character of respiratory type columnar and ciliated epithelium. Examples of this reversal to respiratory type have been frequently observed in both our human and experimental material.[8-10]

Squamous metaplasia is common in the respiratory tract and it would appear to be justifiable to assume that the epithelium of the middle ear in particular when of the respiratory type, may undergo squamous metaplasia in the course of chronic inflammation with suppuration.

It might therefore be of some interest to refer to the changes associated with squamous metaplasia of the bronchial epithelium as described by Auerbach et al.[1]:

Basal Cell Hyperplasia. The first change usually occurs in the form of multiplication of the basal cell layers without the entire loss of columnar cells which can still be easily recognized on the surface.

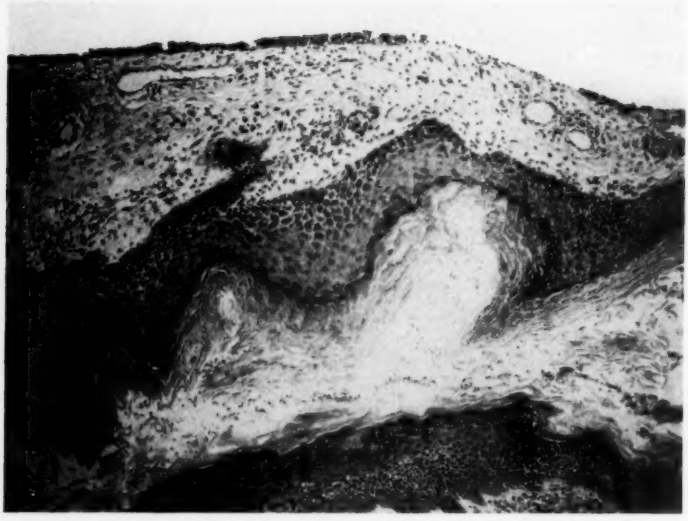


Fig. 4.—Epidermoid Cholesteatoma. Section through the wall of the cyst showing two types of epithelium 1) squamous epithelium forming the cholesteatoma and columnar epithelium of the mucosa of the middle ear. The squamous epithelium must have undermined the normal mucosa and could not have arisen through metaplasia. (H 1327) H. and E. X 190.

Stratification follows when the columnar cells have disappeared and the superficial cells show signs of flattening but no other characteristics of squamous cells.

Squamous metaplasia might ensue, the cells on the surface assuming the characteristics of prickle cells showing intercellular bridges. It is important to note that keratinization has not been observed in squamous metaplasia of the bronchial epithelium.[1] The absence of keratinization in squamous metaplasia of the bronchial epithelium would suggest that even though squamous metaplasia might be encountered in the middle ear this may not necessarily be followed by the formation of an epidermoid cholesteatoma.

Hyperkeratosis of the epidermoid matrix is the *sine qua non* of the histogenesis of epidermoid cholesteatoma.

Mucus glands and ducts of various organs may undergo squamous metaplasia. The phenomenon is not uncommon in salivary

Fig. 5.—Epidermoid Cholesteatoma. Note keratinizing squamous epithelium undermining mucosa covered by cuboidal epithelium. Hematoxylin and eosin X 260 G. 1441

gland tumors or in glands of the oral cavity. In the breast Salm[20] described an interesting case of squamous metaplasia and pointed out that owing to its rare nature its occurrence was unknown to many histologists of great experience. It has been suggested that squamous metaplasia might occur in the gland-like structures encountered in chronic otitis media. Rüedi[19] found no evidence of metaplasia in 124 sectioned temporal bones and it is difficult to accept the evidence presented by Birrell[4] in his illustrations 4 and 5. These show at best stratification of the glandular epithelium which, however, appears to be lacking in the characteristic features of squamous epithelium. It may be repeated that squamous metaplasia cannot be diagnosed in the absence of intercellular bridges or prickle cells.[1]

In common with Rüedi[19] we have found no evidence of squamous metaplasia in the infected suppurating bullae of approximately 600 guinea-pigs infected intraurally with various types of microrganisms even though many bullae have developed a typical respiratory type mucosa lined by columnar epithelium and forming gland-like structures.[8]

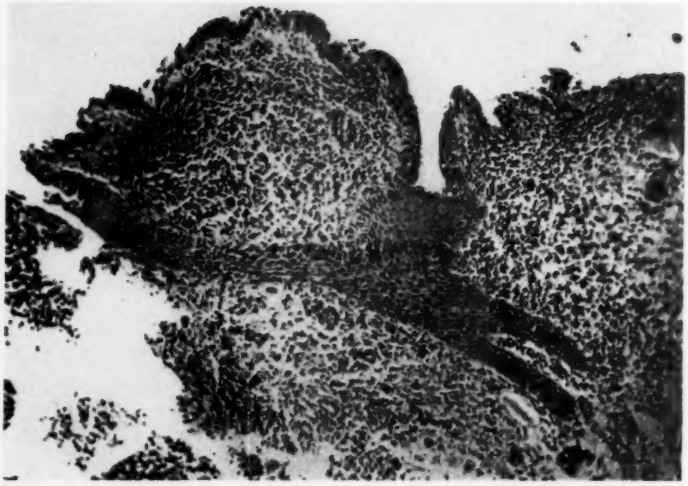


Fig. 6.—Section of granulation tissue removed from middle ear showing tubular gland or duct lined by ciliated columnar epithelium. Note base covered by squamous epithelium which may have reached it from elsewhere but findings strongly suggest squamous metaplasia. (1496/58) Hematoxylin and eosin X 100

5. *Hyperplasia.* Tumarkin's[26] ingenious hypothesis was based on the assumption that the attic was lined with a specific type of epithelium which would in turn become hyperplastic and form the cholesteatoma matrix. The normal attic epithelium, however, is neither stratified nor is it endowed with the property of keratinization. Whether it is possible for cholesterol to be deposited in the attic from desquamated epithelium leading to the development of a cholesterol-granuloma is a point worth considering[27] although this would not in itself explain the development of epidermoid cholesteatoma in the attic.

Nomenclature. The term cholesteatoma was introduced by Johannes Müller[17] in 1838. All through the years this term appears on the whole to have been accepted by most people, but has invited a good deal of speculation and serious study concerning the role of cholesterol in its production and also of its problematic neoplastic nature. Gavin Young[29] in 1950 in a thoughtful attempt at terminological reform introduced "cholesteatosis" thus eliminating the neoplastic suggestion of the previous term but leaving the implied

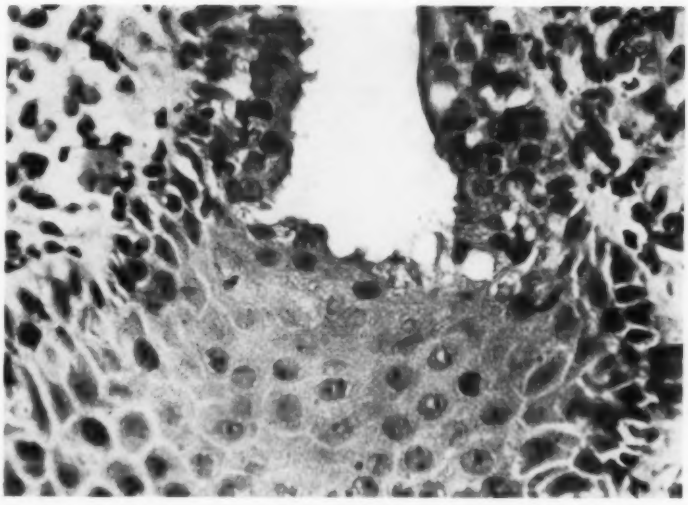


Fig. 7.—Base of gland detail of figure. Note prickle cells showing intercellular bridges. Hematoxylin and eosin X 650 (1496/58)

association with cholesterol open. More recently Tumarkin[27] suggested the word "epidermosis" and Birrell[4] the terms "squamous cholesteatosis" or "squamous epitheliosis." Some of these terms, while eliminating the association with cholesterol, would imply that we are dealing with a disease *per se* of the epidermis or of squamous epithelium.

The present writer has suggested that the term cholesteatoma should be retained so as better to convey the clinical significance of the condition, but used only for epidermoid or keratinous cysts occurring in the ear. This suggestion is supported by Rüedi and Simpson.[19,22] The suggested complete term "epidermoid cholesteatoma" would then be associated exclusively with this important and serious condition of the ear and of no other organ, without necessarily implying an obligate association with cholesterol as an etiological factor; the qualification "epidermoid" indicating its matrix and principal histological component.

It could be argued that it might be best to dispense with the term cholesteatoma altogether and call it, as in fact it is, "the epider-

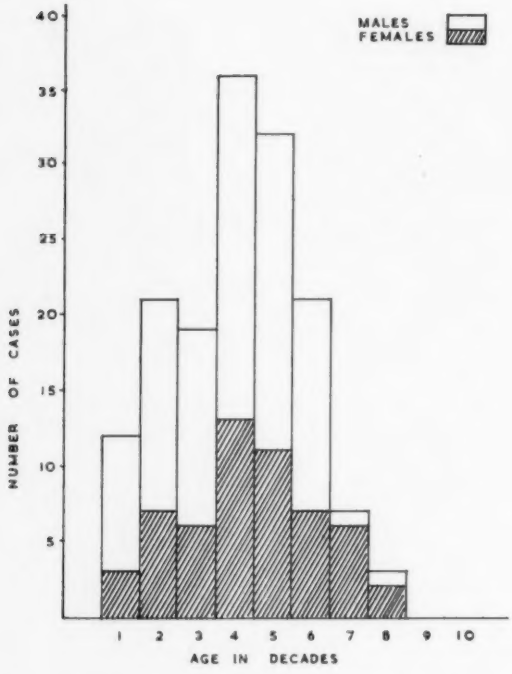


Fig. 8.—Epidermoid Cholesteatoma—age and sex distribution.

moid or keratinous cyst of the middle ear." This is no doubt the most correct description of the pathological findings.

CHOLESTEROL GRANULOMA

Structure. The histopathology of cholesterol-granuloma differs fundamentally from that of the epidermoid cholesteatoma. It is a granulomatous structure formed by variable numbers of cholesterol-crystals (clear cleft-like spaces in sections) surrounded by foreign body giant cells and embedded in fibrous granulation tissue (Fig. 2). There is frequently some fresh blood, more often some blood pigment present, suggesting the pathogenesis of this structure.

Histogenesis. Cholesterol-crystals are deposited at the site of hemorrhage or, rarely, suppuration and acting as irritants may soon attract foreign-body giant cells and provoke fibrosis.

Fig. 9.—Cholesterol Granuloma—age and sex distribution.

Site. It may occur anywhere in the middle ear in the course of chronic otitis media. Thomas[25] has described cholesterol granuloma formation in a fenestration cavity.

NOMENCLATURE

Cholesterol granuloma in the ear appears to have been first described by Manassé[16] in 1917 but attracted little attention until Singer[23] rediscovered it. However, recent literature and textbooks have ignored this interesting feature of the pathology of chronic otitis media. Birrell[3] in a paper entitled "Black Cellular Cholesteatosis in Children" included beautiful illustrations of cholesterol-granulomata but misinterpreted them as cholesteatomata or black cholesteatoma.

On histopathological grounds the present writer has recommended the adoption of the term cholesterol-granuloma for these structures[9,10] without implying that it was a clinical or pathological entity. It must be stressed that the term itself is a histological one and inapplicable as a clinical diagnosis. As such it does not seem to be justifiable to diagnose clinically a case of cholesterol-granuloma or black cholesteatoma. The cholesterol-granuloma is an element of the granulation tissue formed in the course of middle ear infections and can only be recognized with accuracy in sectioned material removed at operation (Table III).

EPIDERMOID CHOLESTEATOMA AND CHOLESTEROL GRANULOMA

As both conditions can occur simultaneously (Fig. 3), it is not surprising that cholesterol crystals have been found in sectioned ma-

terial removed at operations on the mastoid process. The microscopical recognition of the cholesterol granuloma should help in clarifying the vexed question of the role of cholesterol in the pathology of chronic infections of the middle ear.

ANALYSIS OF CLINICAL MATERIAL

Specimens of 770 bone-chips removed at operations on the mastoid process in the period 1935-1956 performed at the Royal National Throat, Nose and Ear Hospital, London, systematically investigated. The relevant results are summarized in Tables I to IV and Figures 8 and 9.

TABLE I

HISTOLOGICAL DIAGNOSIS OF 770 BONE CHIPS
(Examined in the period 1953 to 1956)

Acute or Subacute Otitis Media:	38	(4.93%)
Chronic Otitis Media:		
(Granulation tissue, glands, sclerotic changes of bone present but no evidence of epidermoid cholesteatoma, cholesterol granuloma or squamous epithelium)	379	(49.22%)
Epidermoid cholesteatoma:	151	(19.61%)
Epidermoid cholesteatoma & cholesterol granuloma:	13	(1.68%)
Cholesterol granuloma:	43	(5.58%)
Tuberculous otitis media:	7	(0.90%)
Squamous cell carcinoma:	10	(1.29%)
No evidence of disease:	129	(16.79%)

Some of the more significant histological observations may be illustrated here.

Ingrowth of Epithelium. Sections of human material removed at operations on the mastoid process have furnished convincing evidence of the ingrowth of squamous epithelium into the ear. Figures 4 and 5 show squamous epithelium lining the cavity of epidermoid cholesteatoma spreading underneath the mucosa of the middle ear whose cuboidal or columnar epithelium appears to be intact. These and similar findings have suggested the ingrowth of squamous epithelium into the middle ear as otherwise the co-existence, in this form, of the

Fig. 10.—Fragment of vascular bone removed at mastoidectomy operation. Note cystic epidermoid cholesteatoma at the bottom, and two large cholesterol granulomata inside cells or perivascular spaces. (I 1115) X 14

columnar epithelium of the mucosa and of the squamous epithelium could not be explained.

Squamous Metaplasia. Columnar epithelium and gland-like structures have been observed in granulation tissue removed from the middle ear; there was, however, no evidence of squamous epithelium in 379 specimens showing histological signs of chronic infection (Table I).

Nevertheless it might be relevant to mention in this place the findings in a more recently investigated specimen (1496/58) or granulation tissue removed at operation from the middle ear cavity. Figures 6 and 7 show a tubular gland lined by ciliated columnar epithelium the base of which is covered by polygonal prickle cells with intercellular bridges. There is no evidence of keratinization, an essential factor in the formation of epidermoid cysts. The findings are suggestive of squamous metaplasia although the possibility of ingrowth of the squamous epithelium from elsewhere could not be entirely excluded.

TABLE II

CLINICO-PATHOLOGICAL CORRELATION OF 151 MICROSCOPICALLY DIAGNOSED CASES OF EPIDERMOID CHOLESTEATOMA

	TOTAL	EPIDERMOID CHOLESTEATOMA DIAGNOSED
Microscopical Findings	151	151
Operational Findings	151	130
Radiological Findings	104	46

Clinico-Pathological Correlations. Table II indicates the difficulties of the radiological and clinical identification of epidermoid cholesteatoma.

The clinico-pathological correlation of cholesterol granuloma is not easy. In about half of the cases studied (Table III) cholesteatoma was observed at operations but not microscopically. The simultaneous occurrence of epidermoid cholesteatoma and cholesterol granuloma is not uncommon, and has led to some speculation and confusion concerning the role of cholesterol in the formation of epidermoid cholesteatomata (Fig. 3). Both conditions have, however, only one factor in common, that of the underlying chronic infection. Cholesterol granulomata are probably formed long before the development of epidermoid structures, the growth and ultimate breakdown of which may often be measured in decades rather than years.

TABLE III

CLINICO-PATHOLOGICAL CORRELATION OF 43 MICROSCOPICALLY DIAGNOSED CASES OF CHRONIC OTITIS MEDIA WITH CHOLESTEROL GRANULOMA

	CHOLESTEROL GRANULOMA	EPIDERMOID CHOLESTEATOMA	GRANULATIONS OR OTHER EVIDENCE OF INFECTION
Microscopical Findings	43	—	43
Operational Findings	—	20	23
Radiological Findings	—	5	Positive: 7
			Negative: 17
			Not Performed: 14

Duration of Symptoms. Although figures are small it would appear that a higher percentage of cholesterol granulomata presented with a history of less than one year's duration than was the case with epidermoid cholesteatoma (Table IV).

TABLE IV

APPROXIMATE DURATION OF SYMPTOMS PRIOR TO OPERATIVE TREATMENT

DIAGNOSES	NO. OF CASES	LESS THAN ONE YEAR	MORE THAN ONE YEAR
Epidermoid cholesteatoma	151	15	136
Chronic otitis media with cholesterol granuloma	43	12	31

Age and Sex Distribution of 151 Cases of Epidermoid Cholesteatoma and 43 Cases of Chronic Otitis Media with Cholesterol Granuloma (Figs. 8 and 9). The age distribution of 151 histologically confirmed cases of epidermoid cholesteatoma (Fig. 4) shows that although the majority of cases fall within the 20 to 60 age group no age group is exempt. Whereas epidermoid cholesteatoma is considered to be rare among children, 12 of the cases studied were younger than ten years of age, the youngest of which was only four when operated on.

It is likely that these children and younger individuals under the age of 20 (total number 33) have received some antibiotic or chemotherapeutic treatment. Attention is drawn to this group of patients indicating that epidermoid cholesteatoma may still require a good deal of attention in the future.

The age distribution of 43 cases of chronic otitis media with cholesterol granuloma (Fig. 5) also shows a fairly high percentage of younger patients.

Birrell[4] has drawn attention to the interesting fact that cholesterol granulomata may occur in children whose mastoid processes were pneumatized. A recent case seen by us might, therefore, be of some interest. Figures 10 and 11 show a fragment of vascular mastoid bone. There were several cholesterol-granulomata present lying in what appears to be distended perivascular spaces or possibly cells. The patient, a girl of nine, has been suffering from otitis media with discharge 16 months prior to cortical mastoidectomy. There was also

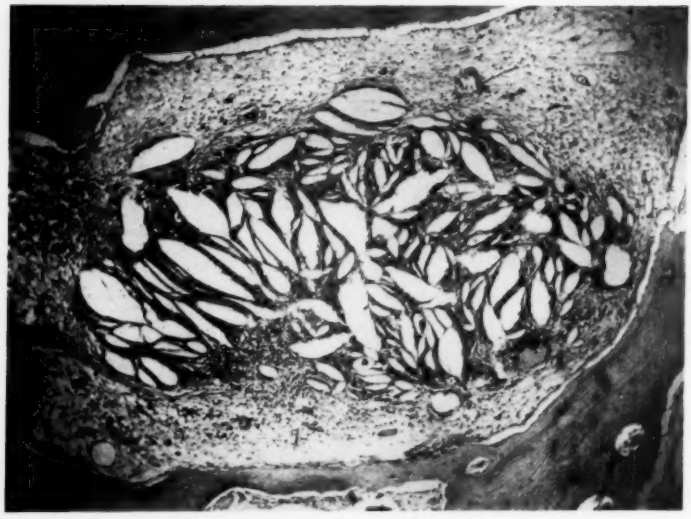


Fig. 11.—Detail of previous section showing cholesterol granuloma inside a cell or distended perivascular space. (I 1116) X 55.

an epidermoid cholesteatoma present as in Rüedi's patient[19] illustrated in his Figure 8 but the two lesions were well-separated from each other.

ANALYSIS OF EXPERIMENTAL MATERIAL

Experimental Epidermoid Cholesteatoma. Experimental evidence in guinea-pigs has previously been presented[9] that keratinizing squamous epithelium may migrate from the external auditory meatus or tympanic membrane into the bulla of the experimentally infected guinea-pig. This occurrence was observed in 10 per cent of the experimentally infected bullae. Figure 12 shows the bulla of a guinea-pig after intraural infection with Pseudomomas pyocyanea (Strain Py. 2800), and the characteristic picture of epidermoid cholesteatoma. The squamous epithelium of the external auditory meatus has spread far into the bulla and formed the matrix of the epidermoid cholesteatoma. Similar findings were observed in the elegant experiments of Rüedi who used a surgical approach to the bulla leaving the tympanic membrane intact.

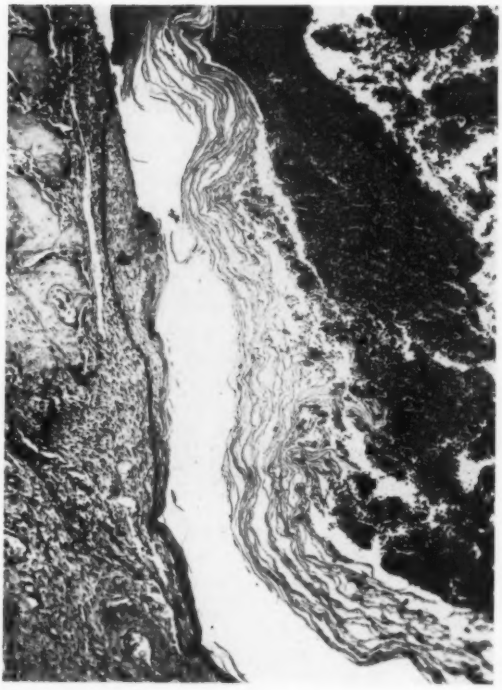


Fig. 12.—Experimental Epidermoid Cholesteatoma of guinea pig, following infection with Ps. Pyocyanea. Note bulla wall covered by ingrowing squamous epithelium and desquamated layers of keratin of epithelium and pus in the cavity. (G.P. 644) X 180.

ATTEMPTS AT EXPERIMENTALLY INDUCED METAPLASIA

The Effect of Estrogens. Bonser (1954) has shown that in animal experiments an abundant supply of estrogens may promote squamous metaplasia and keratinization in the bladder. Estrogen-induced uterine metaplasia and keratinization has also been described by Bo et al.[5] and others.

We have treated 24 guinea-pigs with subcutaneous or intramuscular injections of estrogens (Ovocyclin P or M, Ciba) but squamous metaplasia in the bulla was not observed at this estrogen level although some animals showed uterine squamous metaplasia. Twelve guinea-pigs were infected with Pseudomonas pycocyanea (Strain

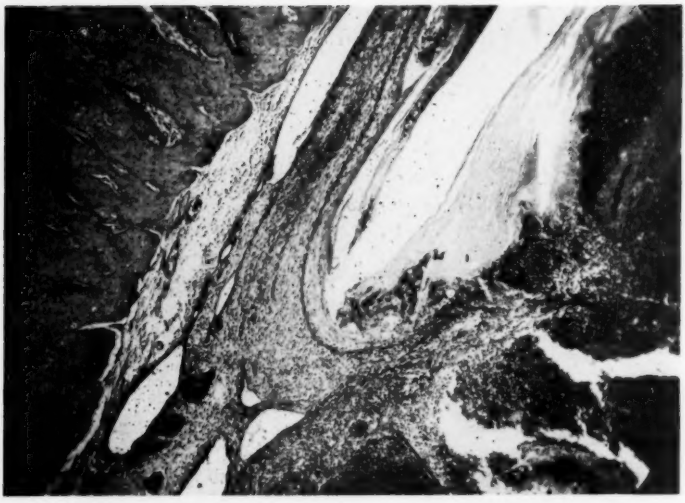


Fig. 13.—Experimental Epidermoid Cholesteatoma of guinea pig, following injection of Ps. Pyocyanea and Ovocyclin P (5 mgs for 6 weeks). (G.P. 994) X 55.

Pyo 26) and then treated with Ovocyclin P 5 mgms for six weeks (in weekly doses). Two of these animals developed typical epidermoid cholesteatoma almost certainly of the migratory type (Fig. 13).

The Effect of Cholesterol. There has been some speculation whether cholesterol deposits might cause squamous metaplasia. In our experience cholesterol suspensions injected into the bullae of guinea-pigs failed to cause metaplasia although, as will be mentioned, cholesterol granuloma formation has been observed in our experimental animals.

Experimental Cholesterol Granuloma. In common with Rüedi[19] we have never seen a cholesterol-granuloma in experimentally infected ears. Similar structures could, however, be reproduced experimentally after the injection of sterile suspensions of cholesterol into the middle ear of the guinea-pig.

The Preparation of Cholesterol Suspensions. 0.5 ml of a saturated solution of cholesterol in equal parts of absolute alcohol and ether are added to 2 ml sterile saline and then shaken vigorously on

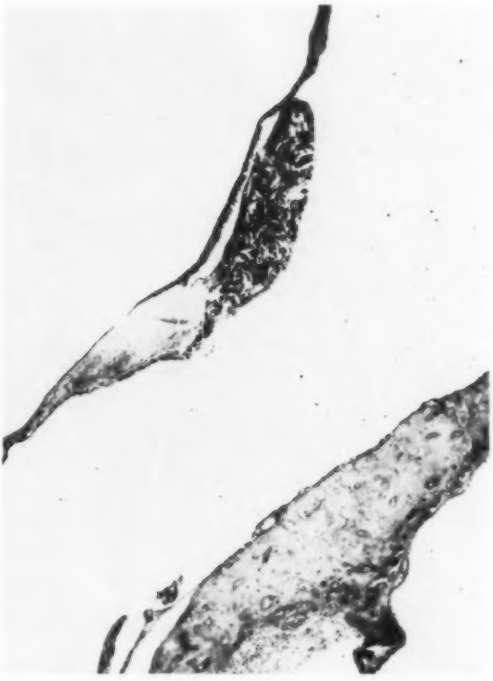


Fig. 14.—Experimental Cholesterol Granuloma. Note small granuloma with cholesterol clefts attached to the internal surface of the tympanic membrane. (G.P. 836) X 115.

a mechanical shaker for approximately 10 to 20 minutes. This produced a stable suspension for intraural injection. After cleansing and disinfecting the auricle and auditory meatus with spirit, 0.05 to 0.2 ml—according to the capacity of the bulla—was injected through the tympanic membrane in accordance with one of the following schedules:

1) Single dose given; 2) repeated doses given at 5 to 8 day intervals; 3) cholesterol injected into previously experimentally infected ears.

Cholesterol-granulomata have been found, surprisingly enough only in none-infected ears, as small masses of cholesterol-crystals or

Fig. 15.—Experimental Cholesterol Granuloma detail showing cholesterol crystals embedded in inflammatory granulation tissue. (G.P. 836) X 750.

clefts embedded in granulation tissue with foreign-body giant cells. Most commonly they were found in the neighborhood of the needle track behind the tympanic membrane (Figs. 14 and 15) or in more protected parts of the bulla such as between the cochlea and the bulla wall, usually within the first few weeks following injections. There was no trace of residual cholesterol in animals killed later than a month after injection.

COMMENT

From the results of this systematic analysis of current human and experimental material it may, therefore, be concluded that, in the majority of cases, epidermoid cholesteatoma is caused through

ingrowth or implantation of squamous epithelium into the middle ear. The role of squamous metaplasia does not appear to be as important as has been previously assumed, but it ought to be further studied in view of the importance of this phenomenon in the lower respiratory tract.

Attempts at producing squamous metaplasia in the guinea-pig have failed so far either by means of intraural or systemic injections of cholesterol or estrogens in the form of Ovocyclin P and M (Ciba). Hieger[13] in a study of the carcinogenic effect of repeated doses of cholesterol observed the formation of cholesterol-granulomata at the site of injection.

Our experiments have confirmed that cholesterol crystals may act as foreign-body irritants causing the formation of granulomata,[21] for experimental injections of cholesterol crystals into the bulla of the guinea-pig have occasionally led to the formation of structures resembling the cholesterol granuloma of chronic otitis media. There was, however, no evidence of squamous metaplasia nor was the injection of cholesterol ever accompanied by the production of an epidermoid cholesteatoma.

SUMMARY

The histogenesis and nomenclature of epidermoid cholesteatoma and cholesterol granuloma are discussed, based on a systematic investigation of current clinical and experimental material. Evidence is presented in support of the validity of the immigration theory of the pathogenesis of epidermoid cholesteatoma. The role of squamous metaplasia is discussed and attention is drawn to the frequent absence in metaplastic squamous epithelium of keratinization, a *sine qua non* of the pathogenesis of epidermoid cholesteatoma.

The term epidermoid cholesteatoma is advocated, reserving the term exclusively for epidermoid cysts of the middle ear as it might be more accurately described, with the qualification "epidermoid" indicating its histological background. The role of cholesterol is discussed and the cholesterol granuloma is described. It is stressed that cholesterol granuloma is not a clinical entity and can accurately be recognized only microscopically.

Experimental cholesterol granuloma was observed in the bullae of guinea-pigs following the injections of sterile cholesterol-suspensions.

Attempts at producing squamous metaplasia in the bullae of the guinea-pig with intraural application of cholesterol or systemic injections of estrogens have been unsuccessful but will be continued.

330 GRAY'S INN ROAD

The author is grateful to the surgical staff of the Royal National Throat, Nose and Ear Hospital (London) for their kind co-operation; to Miss V. F. Shepherd for the histological sections and to Mr. D. Connolly for the photomicrographs.

REFERENCES

1. Auerbach, O., Petrick, T. G., Stout, A. P., Statsinger, A. L., Muehsam, G. E., Forman, J. B., and Gere, J. B.: The Anatomical Approach to the Study of Smoking and Bronchogenic Carcinoma; A Preliminary Report of Forty-one Cases. Cancer, N.Y., 9:76, 1956.

2. Beichert, F.: Das Lappencholesteatom. Z. Laryng. Rhinol. 37:567, 1958.

3. Birrell, J. F.: Black Cellular Cholesteatosis in Childhood. J. Laryng. 70:260, 1956.

4. Birrell, J. F.: Cholesteatosis of the Attic. J. Laryng. 72:620, 1958.

5. Bo, W. J.: Histochemical Observations on Metaplastic Epithelium of the Rat Uterus. A.M.A. Arch. Path. 64:601, 1957.

6. Choremis, C., Economos, D., Papadatos, C., and Gargoulas, A.: Intraspinal Epidermoid Tumours (Cholesteatomas) in Patients Treated for Tuberculous Meningitis. Lancet 2:437, 1956.

7. Cruveilhier, J.: Anatomie pathologique du corps humain. 1:341, Paris, 1829.

8. Friedmann, I.: The Comparative Pathology of Otitis Media—Experimental and Human. I. Experimental Otitis of the Guinea-pig. J. Laryng. 69:27, 1955a.

9. Friedmann, I.: The Comparative Pathology of Otitis Media—Experimental and Human. II. The Histopathology of Experimental Otitis of the Guinea-pig with Particular Reference to Experimental Cholesteatoma. J. Laryng. 69:588, 1955b.

10. Friedmann, I.: Pathology of Otitis Media. J. Clin. Path. 9:229, 1956.

11. Friedmann, I.: Epidermoid Cholesteatoma and Cholesterol Granuloma of the Ear. Lancet 1:639, 1957.

12. Habermann, J.: Zur Entstehung des Cholesteatoms des Mittelohrs. Arch. Ohr.-, Nas.- u. KehlkHeilk. 27:42, 1888.

13. Hieger, I.: Personal communication.

14. Hieger, I., and Orr, S.F.D.: On the Carcinogenic Activity of Purified Cholesterol. Brit. J. Cancer 8:274, 1954.

15. Keratinous Cysts in the C.N.S. Lancet (leading article) 1:358, 1957.

16. Manassé, P.: In Ohrenheilk. Gegenw., vol. 9, Handbuch der Pathologischen Anatomie des Menschlichen Ohres, p. 51, Wiesbaden, 1917.

17. Müller, J.: Über den feinern Bau und die Formen der Krankhaften Geschwülste 1:50, Berlin, 1838.

18. Rüedi, L.: Pathogenesis and Treatment of Cholesteatoma in Chronic Suppuration of the Temporal Bone. ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY, St. Louis, 66:283, 1957.

19. Rüedi, L.: Cholesteatosis of the Attic. J. Laryng. 72:593, 1958.

20. Salm, R.: Epidermoid Metaplasia in Mammary Fibro-adenoma with Formation of Keratin Cysts. J. Path. Bact. 74:221, 1957.

21. Schröer, R.: Zwei traumatische Mittelohrcholesteatome. Z. Laryng. Rhinol. 37:573, 1958.

22. Simpson, R. R.: Discussion on Cholesteatosis of the Attic. J. Laryng. 72: 684, 1958.

23. Singer, L.: Uber entzundliche erkrankungen des Mittelohres und der pneumatischen Hohlräume des Schläfenbeines. I. Mitteilung: Eine morphologische Studie mit fetalen und post-natalen Beiträgen zur Entwicklung der Mittelohrräume mit Betrachtungen zur vollständingen und unvollständingen Pneumatisation des Schläfenbeines. Z. Hals- Nas.- u. Ohrenheilk. 32:110, 1933.

24. Stewart, M. J.: On the Occurrence of Irritation Giant Cells in Dermoid and Epidermoid Cysts. J. Path. Bact. 17:502, 1913.

24a. Stewart, M. J.: On the Cellular Reactions Induced by Local Deposits of Cholesterin in the Tissues. J. Path. Bact. 19:305, 1915.

25. Thomas, R.: Fenestration Post-mortem Histology. J. Laryng. 72:699, 1958.

26. Tumarkin, A.: Chronic Otorrhoea. In Ellis, M. (Ed.): Modern Trends in Diseases of the Ear, Nose and Throat. 159, London, 1954.

27. Tumarkin, H.: Attic Cholesteatosis. J. Laryng. 72:610, 1958.

28. Tytus, J. S., and Pennybacker, J.: Pearly Tumours in Relation to the Central Nervous System. J. Neurol. Psychiat. 19:241, 1956.

29. Young, G.: Aural Cholesteatoma—or Cholesteatosis; A Review. Proc. R. Soc. Med. 43:75, 1950.

IV

TREATMENT OF SINUS BAROTRAUMA

RALPH N. KRAUS
COLONEL, USAF (MC)
RANDOLPH AIR FORCE BASE, TEXAS

Although numerous papers concerning sinus barotrauma appeared during and immediately following World War II, there has been a paucity of papers on this subject during the past ten years. Nevertheless, the problem of barotrauma remains with us. It is believed that a review of treatment procedures and the presentation of some unusual cases are timely.

Sinus barotrauma is an acute or chronic inflammation of one or more of the nasal accessory sinuses produced by barometric pressure differential between the air or gas inside the sinus and that of the ambient atmosphere.[1] Sinus barotrauma was reported by 3 to 4 per cent of subjects who had altitude indoctrination during World War II. The incidence of sinus pain in chamber flights at the School of Aviation Medicine, USAF, over the past five years has been 2.4 per cent in 3,855 trained flying personnel and 3.5 per cent in 3,440 prospective flight surgeons, most of whom had never flown nor been in an altitude chamber.[3] During 1955 there were 200 temporary suspensions from flying for this condition in the U. S. Air Force; there were no permanent suspensions during this period.[4]

In a study of 100 cases of sinus barotrauma in the Royal Air Force the frontal sinus was involved in 70, the maxillary sinus in 19, the frontal and antrum in ten, and the ethmoid in one.[5]

PHYSIOLOGY

Sinus barotrauma may occur during either ascent or descent, or during both. Symptoms are more likely to occur on descent. As we ascend, the atmospheric pressure decreases. Obstruction to the ostium of a sinus may prevent the escape of air. As ascent is continued, a relative positive pressure occurs within the affected sinus.

On descent the atmospheric pressure increases. Obstruction to the ostium of a sinus will prevent the return of air to the sinus. A

relative negative pressure occurs within the sinus. It has been the author's clinical observation that a relative negative pressure within a sinus is more painful than an equal amount of positive pressure. Pathologic conditions are more likely to prevent return of air to the sinus; hence, more people report sinus pain on descent. It is worthy of mention that pain from maxillary sinus pathology may be referred to the frontal region.[7,8] The common cold, sinusitis, allergy, and polyps are some of the common causes of obstruction of a sinus ostium.

PATHOLOGY

The pathology of the milder and moderate degrees of sinus barotrauma is simply that of inflammation ex vacuo consisting of engorgement of the blood vessels, some diapedesis, and generalized submucosal edema with serous fluid in the interstices.[1] The more severe degrees of tissue alteration are those of mucosal detachment and submucosal hematoma. Figure 1 demonstrates a hematoma of the roof of the right maxillary sinus. This patient was treated by infraction of the middle turbinate and then observed for a period of 60 days, during which time the size of the hematoma gradually decreased. Figure 2 demonstrates this decrease in size. After this period the patient tolerated ascent to 30,000 feet at the rate of 6,000 feet a minute and descent at the same rate without symptoms. He was returned to flying status and has had no difficulty since.

TREATMENT

When a patient with sinus barotrauma presents himself for treatment the history, examination, transillumination, and x-rays of the sinuses aid in the diagnosis. Often the findings during the examination are disappointing; little can be detected that is abnormal.

The goal of treatment is restoration of normal physiology to the affected sinus. In most instances nasal shrinkage suffices to reduce the swelling that blocks the ostium. In others, specific anatomic or pathologic conditions must be corrected before normal sinus ventilation can take place.[2] The following regimen has been found successful in helping the patient obtain relief from acute barosinusitis:

1. Nasal shrinkage followed by insertion of a cotton pledget containing a vasoconstrictor into the middle meatus should be tried first.

2. This should be followed by a Proetz displacement procedure.[6] If no relief of the excruciating pain is obtained after a reasonable

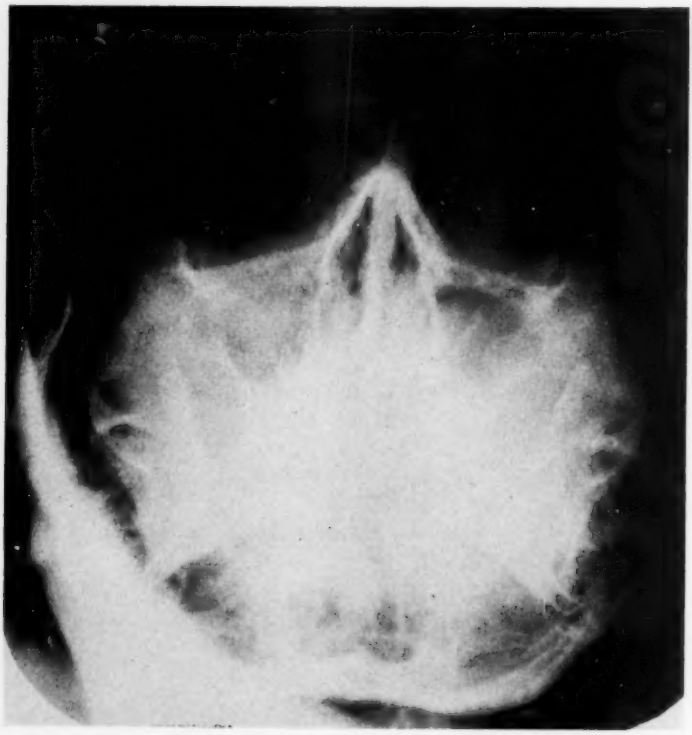


Fig. 1.—Note the triangular-shaped area of increased density in the right maxillary sinus. The base of the triangle extends along the entire roof of the sinus. The apex of the triangle is near the floor of the sinus.

period (20 to 30 minutes), retraction of the middle turbinate should be suspected.

3. Infraction of the middle turbinate. The middle meatus should be anesthetized with a topical anesthetic. A Freer elevator or similar instrument should be inserted into the middle meatus and the middle turbinate infracted. This simple surgical office procedure, which will relieve pain in most cases, has not been given the attention it deserves.

4. Instrumentation of the sinus. In rare instances it may be necessary to cannulate the maxillary sinus through the natural ostium or to puncture the inferior meatal wall with a Lichtwitz needle. The

latter procedure is preferred by the author. Air will return to the sinus through the needle and immediately relieve the negative pressure. While these procedures may seem radical, radical measures are necessary at this point to relieve the pain and to prevent further damage to the sinus mucosa from the negative pressure within the sinus. The quicker the atmospheric pressure within the sinus is neutralized, the sooner the sinus will return to normal.

5. A systemic vasoconstrictor such as ephedrine (gr ⅜), propadrine (gr ⅜), or sudafed 60 mg should be given immediately and repeated three times a day until all signs of nasal congestion have disappeared.

6. Antibiotics should be given systemically in all instances in which sinus infection is suspected.

7. Antihistamines should be given when allergy is either found or suspected.

8. Severe symptoms may be prevented by returning the patient to a higher altitude as soon as symptoms appear; the descent should then be made very slowly. This method is often impractical, however, particularly for passengers in aircraft. Decompression in an altitude chamber followed by a slow descent is likewise effective.

In addition to the conditions usually responsible for interference with sinus ventilation the following conditions have been observed: 1) retraction of the middle turbinate due to deflection of the nasal septum, 2) retention cyst of the maxillary sinus, and 3) osteoma of the frontal sinus.

DEFLECTION OF THE NASAL SEPTUM

In some cases it is impossible to infract the middle turbinate because a deflection of the nasal septum impinges upon the turbinate. In these instances recurring episodes of aerosinusitis should be an indication for a submucous resection and infraction of the middle turbinate. The following case history illustrates this point.

The patient developed pain over the right frontal sinus during jet penetration on his first jet flight three or four years ago. Afterwards he had a similar pain on approximately half of the jet penetrations. Jet penetration is a routine flying maneuver for descent from high altitude, usually carried out in preparation for landing. After

Fig. 2.—This is an x-ray of the same patient as shown in Figure 1. Note that, after 60 days, the area of increased density has decreased in size. It is still present as a semilunar shadow at the roof the sinus.

clearance from Air Traffic Control, the aircraft is "nosed over" and it descends at a rate exceeding 6,000 feet a minute until the desired altitude is reached. The cabin altitude does not change as rapidly because the cabin is pressurized. The actual rate of change of cabin altitude depends on the amount of pressurization.

X-rays of the patient's sinuses one year ago revealed no significant abnormality. The ear, nose and throat examination was within normal limits with the exception of the nose. The nasal septum was deflected to the left inferiorly and to the right superiorly in the mid-portion. The septum was in contact with the right middle turbinate,

Fig. 3.—Note the area of increased density in the right maxillary sinus. It is smooth and dome-shaped near the roof of the sinus and almost completely fills the sinus.

making it impossible to infract the turbinate. The mucosa appeared normal. Sinus x-rays at the time of the present examination revealed a clouding of the right frontal sinus which was probably due to mucosal thickening as a result of repeated barosinusitis. On August 29, 1957, a submucous resection was performed. At the same time the right middle turbinate was infracted. The postoperative course was uneventful. The patient was returned to flying status on September 10. He has had no pain during jet penetration since the operation.

RETENTION CYSTS

Retention cysts of the maxillary sinuses are usually incidental findings on routine sinus films. They may range in size from a few

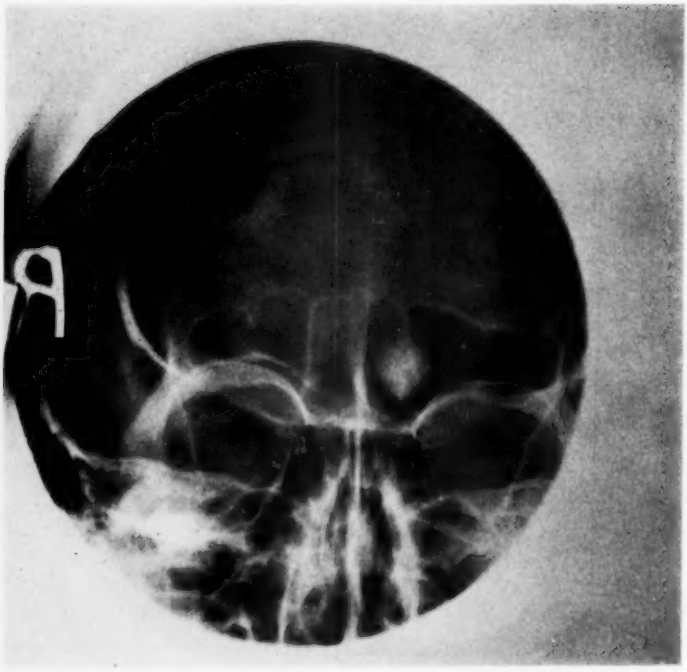


Fig. 4.—Note the osteoma in the left frontal sinus.

millimeters to a size which nearly fills the antrum. They are, in effect, dilated glands from the sinus mucosa. The sacs are lined with ciliated epithelium and are filled with straw-colored, sterile serous fluid.[7]

The following case history describes a retention cyst that was large enough to block the ostium of a maxillary sinus and cause symptoms.

About six months prior to consultation at the School of Aviation Medicine, the patient noticed a numb feeling and pain in his right maxillary teeth upon ascent in an altitude chamber. On each subsequent flight in the F-86D he developed pain at an altitude of 20,000 feet and above (cabin pressure 12,000 feet). He had flown above 12,000 feet many times previously and had experienced no symptoms.

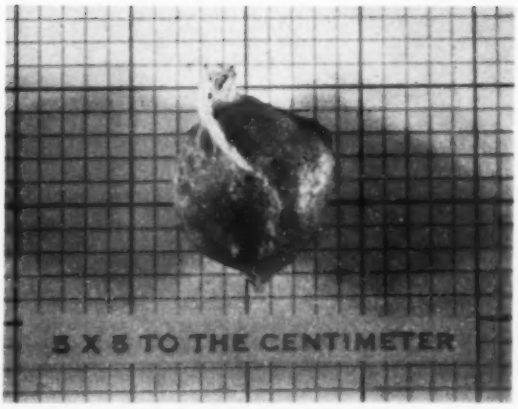


Fig. 5.—The osteoma after removal from the left frontal sinus (Fig. 4).

The pain became unbearable after 15 to 20 minutes. It was not associated with nasal congestion. The pain would rapidly disappear after landing.

The ear, nose, and throat examination was essentially normal. Sinus x-rays in the Waters position revealed a definite clouding of the right maxillary sinus with a smooth domelike surface near the roof (Fig. 3). On August 10, 1955, the cyst was removed by means of a right maxillary sinusotomy. The cyst was found to almost fill the sinus. It would apparently prolapse over the ostium on ascent and prevent the escape of the air between the cyst and the lateral wall of the sinus. Thus a relative positive pressure would build up as ascent continued. The patient was returned to flying status three weeks after removal of the cyst and has been asymptomatic since.

OSTEOMA

An osteoma is often an incidental finding in sinus x-rays. An osteoma may cause symptoms by obstructing the sinus ostium, by pressing on the walls of the sinus, or by eroding into adjacent structures. Childrey (1939) found 15 osteomas in a series of 3,570 radiographs of sinuses. Twelve of the 15 involved the frontal sinus. An osteoma is a slow-growing nonmalignant growth which seldom recurs. These tumors may be hard and ivorylike with few haversian canals or spongy, cancellous in type with many vessels and marrow spaces. A single tumor may contain elements of both types.[5]

The following case history describes an osteoma which contributed to symptomatic frontal sinus barotrauma.

On June 30, 1956, the patient developed pain in his frontal region on descent from 40,000 feet in the altitude chamber. On the afternoon of the same day he flew in a T-33 type aircraft and again suffered pain in the frontal region during descent. The patient was evaluated by a civilian consultant. A history of mild episodes of hay fever was obtained. Skin tests indicated a mild allergy to house dust. The middle turbinates were infracted. The patient developed severe pain over the left frontal sinus on subsequent flights. He was then removed from flying status.

The patient was evaluated at the School of Aviation Medicine during the first part of August 1956. The ear and throat examination was essentially normal. There was no pus or exudate in the nose. The mucosa of the nose did not appear to be allergic. No polyps were seen. X-rays of the sinuses revealed a lesion (1 cm in diameter) of increased density apparently within the left frontal sinus (Fig. 4). Skin tests revealed a 4+ reaction to house dust and a 2+ reaction to marsh elder. The patient was taken for a diagnostic flight in the altitude chamber. On descent from 25,000 feet at the rate of 5,000 feet a minute, he developed left frontal sinus pain at an altitude of 16,000 feet. On August 7, 1956, a left frontal sinusotomy was performed with the patient under general anesthesia. An osteoma was found on the posterior wall of the frontal sinus encroaching on the ostium. The osteoma was removed (Fig. 5). The mucosa of the sinus was thickened over the osteoma and around the ostium. Obstruction of the ostium due to the osteoma and thickened mucosa apparently prevented the return of air on descent. The postoperative course was uneventful. The patient was discharged from the hospital ten days later. On September 27, 1956, he was taken for a diagnostic chamber flight, ascending to 43,000 feet. Following two minutes at 43,000 feet the chamber "free fell" to 33,000 feet and then descended at a rate of 6,000 feet a minute to ground level. The patient experienced no symptoms. He was returned to flying status and has had no difficulty since. He was not treated for the allergy. Absence of symptoms since removal of the osteoma indicate that the osteoma rather than allergy was responsible for the symptoms.

SUMMARY

The physiology and pathology of sinus barotrauma have been reviewed. A successful regimen for treatment has been presented.

The simple office procedure of infraction of the middle turbinate will frequently relieve the acute symptoms and should be tried in recurrent cases in which the cause is not obvious. A submucous resection is indicated when the septum impinges on the middle turbinate and prevents infraction of the turbinate. Examples of sinus barotrauma caused by a retention cyst in the maxillary sinus and an osteoma of a frontal sinus have been presented.

HQ SCHOOL OF AVIATION MEDICINE

REFERENCES

1. Campbell, P. A.: Otolaryngology 3:12, Hagerstown, Md., W. F. Prior Co., Inc., 1955.

2. Campbell, P. A.: Aerosinusitis—Its Cause, Course and Treatment. ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY 53:291, 1944.

3. Personal Communication. Department of Physiology-Biophysics, School of Aviation Medicine, USAF.

4. Personal Communication. Department of Biometrics, School of Aviation Medicine, USAF.

5. Dickson, E. D. D., and King, P. F.: The Results of Treatment of Otitic and Sinus Barotrauma. FPRC 913 (Flying Personnel Research Committee) (Mar.) 1955.

6. Proetz, A. W.: The Displacement Method of Sinus Diagnosis and Treatment. St. Louis: Annals Publishing Co., 1946.

7. Van Alyea, O. E.: Nasal Sinuses. Baltimore: Williams and Wilkins, 1951.

8. Wolff, H. G.: Headache and Other Head Pain. New York: Oxford University Press, 1948.

V

HEARING PROBLEMS ASSOCIATED WITH CLEFT PALATE

MAURICE H. MILLER, PH.D.

BROOKLYN, N. Y.

The association of conductive losses of hearing with cleft palate has been known for many years. However, it was not until recently that controlled audiometric studies of the hearing sensitivity of patients with this condition have been performed and reported in the literature. As these studies of hearing loss in patients with cleft palate are examined, we note certain discrepancies in the incidence of hearing impairments in this group reported by different writers.

In December, 1939, Gaines[1] presented a paper to what was then the American Speech Correction Society dealing with the frequency and effect of hearing loss in cases of cleft palate. The object of her study was to investigate the hearing loss of cleft palate children compared to the hearing loss of a control group of functional articulatory speech defectives having no structural anomalies. Pure tone audiometric tests were performed in the private office of an otologist by a well trained assistant who used a Western Electric 2A audiometer. The experimental group was composed of 44 cleft palate patients, ranging in age from 4 to 13 years with an average age of 8 years and 8 months. The results of this study showed definite differences between the hearing sensitivity of the cleft palate patients and the control group. The comparison showed consistently greater hearing loss in the group of cleft palate patients than in the control group in all the analyses computed. However, the magnitude of the differences between the two groups was not impressive, and Gaines suggests that the differences found may not be statistically significant. For example, the mean percentage loss of hearing for 512-1024-2048 cycles per second for the right ear of the cleft palate patients was 17 decibels, while the mean loss for the control group was 11.7 decibels. This difference of 5.3 decibels between the groups can hardly be considered significant in a study in which only one test was performed on each

From the Division of Otolaryngology, Department of Surgery, State University of New York Downstate Medical Center, Brooklyn, New York (Ira A. Polisar, M.D., Chairman).

subject in an office which was not sound-treated. The author concludes, however, that the loss of hearing is greater in cleft palate cases than in her control group of functional speech defectives.

Sataloff and Fraser[2] in 1952 reported a study of the hearing sensitivity of thirty patients ranging in age from 5 to 16 with cleft palate. These authors used the term "deafness" to designate a hearing loss of 15 decibels or more in at least two frequencies. Testing was performed at octave points from 250 to 8000 cycles inclusive. The authors report that 90 per cent of the thirty patients with cleft palate in the study were found to have hearing losses. The unusually high percentage of children found to have hearing losses is apparently the result of the selective group of patients used in this study. All were very poor patients referred to a clinic for the care of the indigent who had histories of ear infections.

In the latest edition of the Berry and Eisenson[3] text, "Speech Disorders: Principles and Practices of Therapy," Berry reports the results of audiometric and other evaluations of 383 cleft palate children seen at the Rockford College Speech and Hearing Center in 1955 and 1956. Her study indicates that less than 60 per cent of these children suffer from "a recognizable handicap of hearing." The details of the audiometric procedures are not given and we have no way of knowing what the author regards as a recognizable handicap of hearing.

EXPLANATION FOR DISCREPANCIES REPORTED REGARDING INCIDENCE OF HEARING LOSS

A partial explanation for the wide discrepancies in the incidence of hearing loss reported by these and other authors may be found in the semantic confusion which surrounds the use of such terms as "deafness," "hearing loss," and "recognizable handicap of hearing." There is a great difference between having a hearing loss and being hard of hearing. For example, many persons who have been exposed to artillery fire or flying for any length of time have a restricted loss of hearing for the 4,096 cycle frequency with normal hearing throughout the remainder of the frequency range. These persons have a definite loss of hearing. However, they are not hard of hearing since their ability to function satisfactorily in social and vocational situations is not affected. Many persons past the age of 50 have some degree of reduced hearing sensitivity for air and bone conduction for the high frequency range due to presbycusis (4,096 cycles and above). These persons, too, have a definite loss of hearing inasmuch

as their hearing does not fall within normal limits for one portion of the frequency range. However, because the frequencies involved are not critical in understanding conversational speech, they should not be classified as being hard of hearing. Many persons have some degree of hearing loss limited to one ear and are able to function effectively in a majority of listening situations. Persons with slight acoustic trauma dips, mild high frequency losses secondary to presbyacusis, or varying degrees of unilateral losses of hearing, have definite losses of hearing but should not be classified as hard of hearing. This differentiation between loss of hearing and hard of hearing should be made in any statistical study dealing with the incidence of hearing impairment in a given population.

Many cleft palate children have some degree of medically significant loss of hearing which can be detected by careful and complete pure tone audiometric tests. In many of these cases the loss of hearing is limited to high frequencies (8,000-12,000 cycles per second) above the range usually considered important for the understanding of speech. The number of children with cleft palate who are actually hard of hearing is very much smaller. It is of great importance to differentiate such slight, medically significant losses of hearing from a hearing loss of sufficient severity to handicap the patient vocationally and socially in his ability to understand and develop normal speech and language.

SIGNIFICANCE OF HIGH FREQUENCY OBSTRUCTIVE HEARING LOSS

The type of loss found in cleft palate cases is predominantly of the conductive type. This refers to an impairment of some portion of the sound transmission apparatus responsible for conducting sound waves from the outer air into the inner ear. Audiometrically this loss appears first in the high frequencies above the range important for the understanding of speech. These frequencies (8,000, 10,000 and 12,000 cycles per second) are generally not included in pure tone screening audiometry, and this type of early hearing loss may remain undetected until a loss of hearing in the frequencies usually tested occurs.

The American Medical Association has informed examiners of certain dangers involved in testing hearing at these frequencies. In the June 1951 report by the Council on Physical Medicine and Rehabilitation,[4] attention was focused on the following areas of difficulty:

"(a) There is no accepted normal threshold of hearing for any frequency above 8,000 cycles per second; (b) the currently accepted normal threshold of hearing for 8,000 cycles per second is under criticism and will undoubtedly be revised if sufficient reliable data to support the current criticisms are accumulated; (c) in view of the uncertainty about the correct normal value for 8,000 cycles per second, any extrapolation of the normal threshold curve to higher frequencies can be considered as only a rough approximation; (d) the scatter (standard deviation) of thresholds at 4,000 and 8,000 cycles per second is considerably greater than at the lower frequencies; (e) physical measurements of the pressure output of an audiometer begin to be difficult and uncertain at 6,000 cycles per second and are very unreliable at 12,000 cycles per second (American Standard Method for the Coupler Calibration of Earphones, Z 24.9-1949). This is due to purely physical relationships between the wavelength of the high frequency sounds and the necessary dimensions of the "coupler" in which the acoustic pressure is measured; (f) at frequencies above 8,000 cycles per second current audiometric earphones are relatively inefficient and are also subject to large variations from one receiver to the other even among those of the same model; (g) resonances within the ear canal are very important at high frequencies and these resonances vary with the size and shape of the canal and also with minor changes in the placement of receivers over the ears."

For the reasons listed above, the Advisory Committee on Audiometers and Hearing Aids added a stipulation to its minimum requirements for pure tone audiometers for diagnostic purposes, and also for screening audiometers, regarding any test frequencies above 8,000 cycles per second as follows: "If any such frequencies are provided as test frequencies, it must be clearly indicated on the audiometer that any measurements made at such frequencies are only rough approximations." It is the opinion of the Committee that such high frequencies in an audiometer are only of qualitative value and it is misleading to record in decibels any hearing losses above 8,000 cycles per second. The Committee also recommended caution in the interpretation of hearing losses determined at 8,000 cycles per second.

The major areas of difficulty listed by the Committee are, in the opinion of the present author, surmountable by several simple clinical procedures well known to trained examiners. The criticism regarding the currently accepted normal threshold for 8,000 cycles per second is certainly justified. The error is in the direction of this frequency being too intense by about five decibels. This means that minus five decibels in the audiometer should be the zero level. This error is easily overcome by the use of a correction factor of plus five to air conduction readings at this frequency.

The problem involving the physical relationships between the wavelengths of these high frequency sounds and the necessary dimensions of the "coupler" in which the acoustic pressure is measured can also be resolved in the clinical test situation. The wavelength of the sound having a frequency of 8,000 cycles per second is about one and one-half inches. In standard audiometric testing, the diaphragm of the receiver is about one and one-half inches from the eardrum

membrane. When an 8,000 cycle per second tone is fed through the receiver, the external auditory canal and the eardrum act as a closed tube, and because the distance between the receiver and the eardrum and the wavelength of the sound are about equal, a tone which is 180 degrees out of phase with the original sound is reflected back from the eardrum and cancels the original signal.[5] A slight movement of the receiver away from the patient's outer ear may, when this condition occurs, result in a threshold 10 to 15 decibels better than that originally determined. This slight movement breaks up the standing wave pattern by altering the distance between the eardrum and the receiver. The examiner can handle this problem by loosening the earphone receiver when testing frequencies above 6,000 cycles per second and permitting the patient to move the earphone slightly until the best threshold is determined. Standing wave patterns similarly affect the determination of air conduction thresholds at 10,000 and 12,000 cycles per second. The Committee states that current audiometer earphones are relatively inefficient above 8,000 cycles per second and are subject to large variations. The examiner can perform a clinical calibration procedure on his own audiometer at these frequencies and use an appropriate correction factor. The procedure for establishing such a table based upon the mean readings of a group of normally hearing young adult subjects has been described by McConnell and Carhart.[6] In the absence of any accepted normal threshold of hearing for frequencies above 8,000 cycles per second, therefore, the examiner can establish his own standard of normality as he must do when he calibrates the bone conduction oscillator for clinical use.[7] When he establishes his normal values for testing air conduction above 8,000 cycles per second, he uses normally hearing young adult subjects. When he calibrates the bone conduction audiometer, he uses cases of mild to moderate bilateral sensori-neural hearing loss.

Despite the difficulties encountered in testing hearing at these frequencies, valuable diagnostic information may be secured by including 8,000, 10,000 and 12,000 cycles per second in audiometric examinations of cleft palate and other children. Crowe and coworkers[8] at Johns Hopkins have presented a wealth of audiometric data suggesting that the most common hearing defect in children is impairment of thresholds for some or all of the high frequencies above 2,048 cycles. This type of high frequency loss of hearing is also quite common in cleft palate children. In a study of thirty-five cleft palate patients ranging in ages from 3 to 23 years, which was reported in 1956,[9] the present author reported that the type of conductive loss of hearing found most frequently in cleft palate cases was one which affected the high frequencies first (8,000 to 12,000 cycles per

second). A loss of 30 decibels or more at one of the frequencies tested was used as the criterion for hearing loss in this study. Frequencies between 125 and 12,000 cycles per second were tested in a properly sound isolated area. Of the fourteen cleft palate children found to have a purely conductive loss of hearing, twelve of them showed losses limited to the very high frequency range. If proper otological treatment is not instituted, the entire frequency range may become involved resulting in the reduced sensitivity for all frequencies characteristic of advanced conductive losses.

These limited high frequency losses, it must be emphasized, are obstructive and not sensori-neural in nature. Bone conduction at the involved frequencies is normal or better than normal. (Several commercial audiometers permit bone conduction measurements in the 8,000 to 12,000 cycles per second range which the author has found to be of diagnostic value when testing the hearing of children with early conductive losses.) Weber testing with the bone conduction oscillator of the audiometer at these very high frequencies shows lateralization to the ear having the greater air-bone gap, and the Rinne test is negative when the loss exceeds 30 decibels. The traditionally held view that high frequency losses are necessarily of the sensori-neural type is not substantiated by the clinical experience of Crowe and his co-workers at Johns Hopkins and by the present author. It is the relationship between the air and bone conduction curves of the impaired ear that must be used to establish a differential diagnosis of the type of hearing loss present. Examination of the air conduction contour alone does not make possible an accurate differential diagnosis.

The medical significance of these incipient, high frequency conductive losses is not accepted by many clinical audiologists and otologists. The author of a generally excellent, recently published textbook in the field of clinical audiology,[11] for example, considers losses at 4,000 and 8,000 cycles per second in school children to be of little consequence.

"Experience has demonstrated that many school children have losses of 30 decibels or more at only 4,000 and 8,000 cycles per second. Almost invariably an otologist who examines children with this type of high frequency loss finds no demonstrable pathology and nothing in the child's history of significance. Many otologists feel that such high frequency losses are congenital and static (not progressive). Since the success of a hearing conservation program depends on securing the cooperation of the examining otologist, it is important that he feel that his time is well spent. It may be advisable, therefore, for the school audiometrist to assign priorities to the pupils identified as having hearing impairments. Those with losses only at 4,000 or 8,000 cycles per second would be given the lowest priority. Highest priority would be given to pupils who have losses through all the speech frequencies."

Limitations of available otological personnel may necessitate the granting of priority to children whose losses of hearing involve the speech frequency range. However, one important objective of a hearing conservation program must be to detect early losses of hearing and prevent the development of a handicapping loss affecting the child's ability to understand speech. The earliest indication of a medically significant loss of hearing in children is a reduction of hearing sensitivity for the high frequencies above the range involved in speech reception. While children with such limited high frequency losses may not be granted priority in a hearing conservation program, they should certainly receive the benefit of a complete otological examination and appropriate medical or surgical treatment, as indicated.

The present author has made it a policy to refer for otological examination all children with high frequency conductive losses of hearing found on wide range pure tone audiometric testing. It has been his experience that significant medical pathology is invariably found by the otologist when children with such losses are examined. In addition to pure tone air conduction testing at frequencies above 4,000 cycles per second, bone conduction measurements and the Weber and Rinne tests with the bone conduction oscillator are performed at the involved frequencies. It is thus possible to differentiate high frequency conductive losses associated with obstructive pathology from the static, congenital losses referred to by Newby. Furthermore, the otological examination on these children must be accompanied by a careful inspection of the nasopharynx in addition to the usual inspection of the tympanic membranes. Under these conditions, a high incidence of early pathology of the sound conducting apparatus will be detected. Appropriate medical and surgical treatment may then be instituted with an excellent chance of averting the development of a handicapping loss of hearing for speech.

CAUSES OF CONDUCTIVE LOSSES OF HEARING IN CLEFT PALATE PATIENTS

The causes of conductive losses of hearing of the type mentioned in children with cleft palate are as follows:

1. *Lymphoid Hyperplasia in the Nasopharynx.* Crowe, et al[10] believe that high frequency losses of hearing in children are due to regeneration of lymphoid tissue in the nasopharynx which frequently occurs after adenoidectomy. They remind us that lymphoid tissue is an integral part of the mucosa of the nasopharyngeal region, and all of

it cannot be removed even by the most meticulous operation without endangering the patency of the eustachian tube by scar tissue formation. The mucosa that grows out over the wound following adenoidectomy, therefore, contains lymphoid tissue. This tissue may undergo regrowth and hyperplasia with consequent infections of the upper respiratory tract. The use of radiation therapy directed at the remaining lymphoid tissue in the fossa of Rosenmuller and in the region of the nasopharyngeal orifice of one or both eustachian tubes by the otolaryngologist is frequently successful in eliminating this lymphoid tissue and in stabilizing or reducing the high frequency conductive loss of hearing which accompanies this condition. This high frequency loss of hearing does not affect the understanding of speech because the frequencies involved are above the critical speech range. The otolaryngologist and the audiologist should view this limited frequency loss as a warning signal of a serious and handicapping loss of hearing which may follow if proper otological treatment is not promptly instituted. A careful inspection of the nasopharynx should be part of the ear, nose, and throat examination of all children with cleft palate.

Crowe referred to children without cleft palates on whom an adenoidectomy had previously been performed. The situation is far more critical in cases of cleft palate because surgeons have traditionally been unwilling to perform an adenoidectomy and tonsillectomy on these children. It has been felt that any tissue in the area of the oro- or nasopharynx serves to facilitate closure of the nasal port, and that an adenoidectomy might have an unfavorable effect on the speech of cleft palate children. Beatty,[12] for example, stated that "if tonsillectomy is done by any of the accepted methods, natural contractions will, to varying extents, impair speech and the function of the velum in deglutition." Therefore, in spite of the effect of lymphoid tissue on hearing sensitivity in these cases, surgeons have been reluctant to remove the tonsils and adenoids because of possible adverse effects on speech production.

When a decision must be reached in these cases as to whether or not to perform a tonsillectomy and adenoidectomy, I believe that the child's hearing should be the primary consideration. It has been the experience of the present author in carrying out individual speech therapy programs with cleft palate patients that there are few adverse effects on speech production resulting from a carefully performed tonsillectomy and adenoidectomy. The improvement of hearing is often considerable in these cases. By early surgical intervention, it may be possible to prevent the occurrence of a more serious, handicap-

ping loss of hearing. Once functional nasopharyngeal closure has been achieved by the speech therapist, the loss of lymphoid tissue following surgery will usually not impede the progress of speech therapy.

2. *The Abnormal Condition to Which the Eustachian Tube Is Exposed in Cleft Palate Cases.* The eustachian tube in cleft palate children becomes a constant object of infection from food, trauma, and inadequate aeration.[13] These infections readily pass via the eustachian tube to the middle ear, where an acute or chronic otitis media may result with its frequent deleterious effect on the child's hearing. Cleft palate patients have a larger proportion of acute inflammations of the middle ear and a much larger proportion of chronic suppurative and non-suppurative otitis media necessitating more frequent myringotomy than do non-cleft palate patients. Likewise, acute nasopharyngitis and a slightly greater occurrence of upper respiratory infections are found in cleft palate patients than in those without this condition.[14] A major factor in accounting for conductive losses of hearing in cleft palate children is the anatomical deviation of the muscles of the palatopharyngeal valve which impairs the function of the eustachian tube. This impairment of tubal function is considered by Gaines to be the major factor accounting for a great and frequently permanent loss of hearing in cleft palate cases.

3. *Disturbances of Eustachian Tube Function Secondary to Mutilating Surgery.* Some surgeons, during an operation to close the cleft in the soft palate, produce scarring or distortion of the tissues at the nasopharyngeal orifice of the eustachian tube, thus interfering with its normal function of equalizing the air pressure on both sides of the tympanic membrane.[15] Such losses of hearing may be referred to as "surgico-genic" since they result not from the cleft palate condition per se but from surgical procedures sometimes employed in the correction of the physical deformity. This is not a statement against cleft palate surgery but is directed only toward those surgical procedures which secondarily traumatize the nasopharyngeal orifice. The effects on hearing of such procedures may not be evident immediately after surgery and will not be detected until wide frequency diagnostic pure tone audiometry is performed. The association of these losses of hearing with the original operative procedure may thus be unknown to the cleft palate surgeon.

THE CLINICAL AUDIOLOGIST AND THE CLEFT PALATE TEAM

It is gratifying to note that the Bureau for Handicapped Children of the New York City Department of Health in its manual of

Standards of Care for Cleft Palate Rehabilitation Centers in Hospitals[16] recommends that audiometric tests be performed upon every child with a cleft palate at as early an age as possible and if and when needed thereafter. Furthermore, treatment of otolaryngologic conditions found in patients with cleft palate is recognized as a function of the Cleft Palate Rehabilitation Clinic. There should be a clinical audiologist on every cleft-palate team devoted to the total rehabilitation of the patient with this condition.

450 CLARKSON AVE.

REFERENCES

1. Gaines, F. P.: Frequency and Effect of Hearing Losses in Cleft Palate Cases. J. Speech Disorders 5:141-149, 1940

2. Sataloff, J., and Fraser, M.: Hearing Loss in Children with Cleft Palates. Arch. Otolaryng. 55:64, 1952.

3. Berry, M., and Eisenson, J.: Speech Disorders: Princip'es and Practices of Therapy. New York, Appleton-Century-Crofts, Inc., 1956, p. 324.

4. Council on Physical Medicine: Audiometry at Higher Frequencies. J. Amer. Med. Ass. 146:817 (June) 1951.

5. Newby, H. A.: Audiology: Principles and Practice. New York, Appleton-Century-Crofts, Inc., 1958, p. 78.

6. McConnell, F., and Carhart, R.: Influence of Fenestration Surgery on Bone Conduction Measurements. Laryngoscope 62:1269 (Dec.) 1952.

7. Roach, R., and Carhart, R.: A Clinical Method for Calibrating the Bone Conduction Oscillator. Arch. Otolaryng. 63:270-278 (Mar.) 1956.

8. Crowe, S. J., Guild, S., Langer, E., Loch, W., and Robbins, M.: Impaired Hearing in School Children. Laryngoscope 52:790, 1942.

9. Miller, M. H.: Hearing Loss in Cleft Palate Cases. The Incidence, Type and Significance. Laryngoscope 66:1492-1496 (Nov.) 1956.

10. Crowe, et al: *Ibid.*, p. 790.

11. Newby, H.: Op. Cit., p. 210.

12. Beatty, H. G.: Cleft Palate. ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY 55:572, 1946.

13. Sataloff and Fraser: *Ibid.*, p. 61.

14. Gaines, F. P.: *Ibid.*, p. 148.

15. Dunn, F. S., M.D., D.D.S., Chief, Oral Surgery Department, Lenox Hill Hospital, New York City: Personal communication with the author.

16. Standards of Care for Cleft Palate Rehabilitation Centers in Hospitals. Bureau for Handicapped Children. New York City Department of Health. October 1953, p. 11.

VI

LARYNGOCELE AND LARYNGEAL CANCER

L. Pietrantoni

D. Felisati

and

A. Finzi

Milan, Italy

The association between laryngeal cancer and laryngocele has been reported by a number of authors, starting with Marschik in 1927[13] and later on by Zöllner,[19] Cova,[5] Torchiana,[18] Leborgne,[10] Schall,[17] Bonandini,[2] Jackson,[9] Guenzi,[8] Casadesus and Capella,[4] Meda,[14,15] Pagano,[16] Mattioli,[13] Carimati, Gignoux and Moindrot[3,7]; Léroux Robert and Rogeon,[11] Blavier.[1]

According to these authors, the association between laryngocele and cancer of the larynx is uncommon; actually, if a correct technique of radiological investigation of the larynx is adopted, we are often able to observe the presence of a ventricular dilatation associated with the presence of laryngeal carcinoma.

Different interpretations have been proposed in order to explain the co-existence of these two pathological findings: some authors believe it to be occasional, while others consider the laryngocele as dependent upon the presence of the tumor.

Generally, it is believed that, whenever there is an association between cancer and laryngocele, Morgagni's ventricle is affected primarily or secondarily by the new growth.

The incidence of bilateral laryngocele has been reported as being low.

PERSONAL RESEARCH

It has been our aim to report on frequency of laryngocele in cases of laryngeal cancer and on the relationship between these two types of lesions.

From the Ear, Nose and Throat Department of the University of Milan.

To this purpose, we have examined the records of over 1000 patients who underwent laryngectomy for cancer in the Ear, Nose and Throat Clinic of the University of Milan from 1948 until now.

Preoperative radiological and tomographical findings of the larynx were available for 857 of these cases. The presence of laryngocele has been demonstrated from the radiological point of view in 53 cases. (Six of these cases have been reported by Meda.[15])

In view of these findings, we have controlled the macroscopic evidence on laryngeal specimens of the Clinic's museum.

This research has been possible only on 31 larynges out of 53, as 22 specimens had been previously used for other investigations and could not be employed for dissection as required by the present study.

In 12 cases out of 31, the radiological findings pointed to the presence of a monolateral laryngocele, but the macroscopic evidence showed, as will be stated further on, that there existed a bilateral laryngocele, or a monolateral form associated with a contralateral abnormally developed appendix. We may therefore assume that the incidence of laryngocele in laryngeal tumors is higher than we have observed radiologically.

TECHNIQUE

First, site, extension and anatomoclinical type of the tumor have been recorded for every specimen. Then, by means of a medial vertical incision, the larynx has been divided in two halves. Finally, three or more transversal incisions parallel to the glottic plane have been made for each hemilarynx.

It has thus been possible to ascertain the presence of an abnormally developed ventricular appendix or of a laryngocele, to dissect the sac and to establish its size and the relationships with the neoplastic lesion. In some cases sections of the cystic mass have been studied by the pathologist.

RESULTS

In a majority of our 31 cases, the neoplastic lesion was very extensive and had spread to the whole supraglottic or subglottic region.

In 20 cases (64 per cent), the tumor had a monolateral extension, in 11 cases it had already crossed the midline. In 12 out of the

monolateral cases, Morgagni's ventricle was primarily or secondarily affected by the new growth.

The tumor had invaded the ventricle 12 times (seven on the right and five on the left side) in bilateral tumors. Thus 22 hemilarynges pertaining to the 11 cases of bilateral tumors have been considered and ten have been shown to be unaffected.

TABLE I

ANATOMICAL-CLINICAL FORMS OF TUMORS (31 CASES)

Veget.	Infiltr.	Veget.-Inf.	Ulcerated Veg.	Ulcerated Inf.	Ulcerated Veg.-Inf.
5	10	6	1	8	1

Thus, out of 42 hemilarynges invaded by the tumor, 24 cases showed a primitive or secondary invasion of the ventricle.

No particular relationship with the anatomoclinical type of the tumor, with its site and extension, could be shown. Lesions were of a fungating or infiltrating type or else mixed forms; ulcerated and non-ulcerated varieties have been present in our series (Table I).

TABLE II

INCIDENCE OF LARYNGOCELE OR OF VENTRICULAR APPENDIX IN MONO- AND BILATERAL TUMORS

	MONOLATERAL	BILATERAL
Tumor	20/31 (64%)	11/31 (36%)
Laryngocele	4/31 (13%)	27/31 (87%)

TYPES OF LARYNGOCELE

The presence of an abnormally developed appendix or of a laryngocele has been shown 58 times; as a matter of fact, a bilateral lesion has been found in 27 cases (87 per cent) and a monolateral one in 4 (13 per cent).

The high incidence of bilateral laryngoceles is rather remarkable, if we consider that, in the majority of our cases, the tumor was monolateral (Table II).

Thus it becomes evident that, in a large majority of our cases, the ventricular appendix occurred on the side opposite to the lesion. In our case material, the bilateral ventricular dilatation was present in 18 out of 20 cases of monolateral tumor.

We shall deal later on with this finding, when discussing the relationships between tumors and laryngocele.

As regards the type of laryngocele, we have found the following distribution: appendix, 14 cases; internal laryngocele, 36 cases; external laryngocele, 8 cases.

ANATOMICAL RELATIONSHIPS BETWEEN LARYNGOCELE OR APPENDIX AND TUMOR

We have investigated whether the tumor was connected with the ventricular dilatation or its appendix, thus pointing to an etiologic relationship between the new growth and the development of the laryngocele.

TABLE III

"Stopple like" tumor occluding the opening of the appendix	T. exerting pressure or invading appendix	T. ex. pressure or invading sacculus of laryngocele	T. ex. pr. or inv. both sacc. of lar. and its app.	No relation between t. and laryngocele
2	19	6	7	24

The examination of specimens has shown that the appendix or the laryngocele and the tumor were related in one of the following ways:

1) The ventricular tumor affects the orifice of the sacculus.

2) The tumor exerts a pressure or invades the appendix.

3) The tumor exerts a pressure or invades the sacculus of the laryngocele.

4) The tumor exerts a pressure or invades the sacculus of the laryngocele and its appendix.

Table III shows the findings as seen in 58 laryngoceles or appendix.

As results from this table, the laryngocele or the abnormally developed appendix showed definitely no relationship with the tumor in 24 cases out of 58. On the contrary, in the remaining 34 cases, the development of the laryngocele seemed basically dependent upon the existence of a tumor spreading to the ventricle or to the neighboring region.

However, in six cases where the tumor affected only the cyst and not its appendix, it was difficult to believe that a check valve mechanism, like the one due to an obstacle to the air flow through the appendix, had been present (Table IV).

TABLE IV

POSSIBLE ETIOLOGICAL RELATIONSHIP BETWEEN TUMOR AND LARYNGOCELE OR APPENDIX

+	−
28 (48%)	30 (52%)

From the etiological point of view, we have thus seen 30 (24 + 6) laryngoceles or appendix cases where it was practically impossible to admit a relationship between the tumor and the laryngocele.

ANATOMICAL-CLINICAL TYPES OF TUMORS IN CASES OF VENTRICULAR HERNIATION BEING RELATED TO THE TUMOR ITSELF

This investigation has failed to reveal the existence of any particular type of tumor (infiltrating, vegetating, mixed, with or without ulceration) related frequently with the development of a ventricular herniation.

COMMENT ON RESULTS

First, it should be pointed out that, in contrast with data reported in the literature, the incidence of laryngocele in laryngeal tumors is not so low.

In our case material, out of 857 cases of laryngeal carcinoma, whose complete roentgenological records had been available, 53 (6.18

per cent) showed radiological signs of mono- or bilateral ventricular herniation (the monolateral type being more frequent).

Owing to the fact that, as shown by our experience, the roentgenological investigation often fails to show the existence of a ventricular dilatation or of an abnormally developed appendix, it might be assumed that the percentage of 6.18 per cent is actually higher.

The low incidence reported by other authors might be due to the technique of roentgenologic investigation, which in some cases cannot reveal the radiotransparent picture of the sacculus communicating with Morgagni's ventricle.

Secondly, we should like to point out that in many cases of association between cancer and laryngocele, Morgagni's ventricle is not affected by the tumor. In our cases material a primitive or secondary localization to the ventricle has been observed only in 24 (57 per cent) out of 42 hemilarynxes invaded by a new growth.

As far as the etiologic relationship between tumor and laryngocele is concerned, we know that a laryngocele usually arises from an abnormally developed ventricular appendix. It is our opinion that frequently the onset and the development of a laryngocele are not directly influenced by the tumor.

The study of our specimens showed not only that in 18 out of 42 hemilarynxes the new growth did not affect in any way the ventricle, but further that frequently bilateral laryngoceles occur in association with strictly monolateral tumors (18 cases out of 20). There was no definite relationship between the tumor and the ventricular appendix even in cases of laryngocele occurring on the same side of the tumor and finally we have observed the presence of an appendix on the same side of a strictly monolateral tumor while on the opposite side there existed a laryngocele.

It may thus be assumed that other factors, related to the presence of the tumor, are responsible for the genesis of this lesion, such as hoarseness, cough, chronic inflammation and all other pathological conditions due to dysphonic and breathing disorders which may cause an increase of pressure in Morgagni's ventricle.

All these causes may have as a consequence a ventricular herniation, whenever there exists an anatomical anomaly such as a ventricular appendix.

SUMMARY

The problem of association between laryngeal cancer and laryngocele has been discussed from the point of view of the incidence of this condition and of the interrelationship between the two types of lesions.

Out of 857 cases of laryngeal cancer, the radio- and tomographical investigation has shown the presence of laryngocele in 53 cases. A study of the specimens has been possible in 31 of these cases.

The results of a macroscopic and histological study have yielded the following data:

1. Incidence of laryngocele in cases of laryngeal cancer, as shown by radiological data, reaches 6.18 per cent. If we consider that the roentgenological investigation often fails to reveal the existence of a ventricular herniation, we are inclined to believe that the said percentage is actually much higher.

2. The ventricle was affected by the tumor in 24 out of 42 hemilarynxes examined (57 per cent).

3. Laryngocele is not always dependent upon the new growth, as shown by the occurrence of monolateral tumors associated with bilateral laryngoceles or even of strictly unilateral tumors accompanied by a ventricular appendix on the same side and by a laryngocele on the opposite side.

4. Most probably, other factors play a role in the onset of laryngocele: first, a predisposing anatomical factor; secondly, the onset of cough, dysphonia and other respiratory and phonatory alterations due to the presence of the tumor, which may cause a rise of pressure in Morgagni's ventricles.

Via Commenda No. 16

REFERENCES

1. Blavier, A.: Un cas de cancer du larynx associé a une laryngocele. Acta O.R.L. Belgica 66:307, 1957.

2. Bonandini, B.: Laringocele e cancro (Osservazioni istopatologiche e cliniche). Il Valsalva 22:1, 1946.

3. Carimati, A.: Il laringocele sintomatico latente (contributo radiologico e clinico). Arch. Rad. 4, fasc. 4, 1956.

4. Casadesus, F., and Capella, G.: Laryngocele: 4 Cases. Acta O.R.L. Ibero-Amer. 2:5, 1951.

5. Cova, P. L.: Sulla dimostrazione radiologica dell'appendice del ventricolo laringeo del Morgagni. Radiol. Med. 28:313, 1941.

6. Felisati, D., Finzi, A., Gattoni: Laringocele e laringits cronicle. Arch. It. O.R.L., in press.

7. Gignoux, M., and Moindrot, M.: Cancer du larynx et laryngocele. Jour. Franc. O.R.L. 581, 1957.

8. Guenzi, L.: Laringocele associato a cancro della laringe. Arch. It. O.R.L.

9. Jackson, Chevalier L.: Laryngocele. Laryng. 57:788, 1947.

10. Leborgne: Reported by Leroux-Robert e Rogeon.

11. Leroux, Robert J., and Rogeon, A.: Tumeurs laryngées et laryngocèle. Annales d'O.R.L. 74:885, 1957.

12. Marschik: Sekundare Laryngocele bei Carcinoma laringis. Zentr. H. N. 10: 104, 1927.

13. Mattioli, V.: Il laringocele. Boll. Mal. O. G. N. 73:337, 1955.

14. Meda, P.: Dimostrazione radiologica del laringocele sintomatico nel cancro della laringe. Atti Soc. Lomb. Sc. Med. Biol. 7:43, 1951.

15. Meda, P.: Symptomatic Laryngocele in Cancer of the Larynx. A.M.A. Arch. of Otolar. 56:512, 1952.

16. Pagano, A.: Laringocele bilaterale e cancro della laringe. Arch. It. Laring. Suppl. Vol. 62:57, 1954.

17. Schall, LeRoy A.: Laryngocele Associated with Cancer of the Larynx. Ann. of O.R.L. 53:168, 1944.

18. Torchiana, L.: Laringocele e cancro della laringe. O.R.L. It. 12:416, 1942.

19. Zollner, F.: Uber das Kehlsackempyem. Beitr. Anat. Physiol. Path. Therap. d. Ohres 30:274, 1932.

VII

THE USE OF THE SCANOGRAPH IN THE DIAGNOSIS OF MASSES AT THE BASE OF THE TONGUE

JAMES A. HARRILL, M.D.
JOSEPH E. WHITLEY, M.D.
I. MESCHAN, M.D.
WINSTON-SALEM, N. C.

The differential diagnosis of masses presenting at the base of the tongue in infants and children most often lies between a thyroglossal duct cyst, accessory thyroid tissue, and an ectopic thyroid gland. Preoperative differentiation of these conditions is critical in the consideration of their surgical treatment. Biopsy is often hazardous, as bleeding in this location is sometimes difficult to control. If thyroid tissue is observed histologically, no knowledge is obtained as to whether the mass represents the entire thyroid gland or the accessory thyroid tissue left behind in the embryonic migration of the thyroid.

The affinity of normal thyroid tissue for iodine in a normal or ectopic location makes possible its differentiation and delineation by radioisotopic technique. Scanograms of the oral pharynx and neck 24 hours after oral administration of a tracer dose of I^{131} are employed in such cases prior to consideration of biopsy. The scans are performed on Polaroid, anteroposterior and lateral views of the neck for ease of interpretation.[1]

The instrument employed is a Nuclear of Chicago Model 1700 Isotope Scanner with a Radiation Counter Laboratory detection head with a 1″ x 1″ sodium iodide thallium activated crystal; Bell and Francis "honeycomb" focusing collimator and Radiation Counter Laboratory Model 2207 Medical Spectrometer.

The dose administered is calculated according to the weight of the patient so as to yield less than 300 milliroentgens in the first

From the Department of Otolaryngology, Bowman Gray School of Medicine of Wake Forest College, the Department of Radiology, North Carolina Baptist Hospital and the Department of Radiology, Bowman Gray School of Medicine of Wake Forest College.

Fig. 1.—Scans obtained in the lateral projection on Case No. 26-47-81.

Fig. 2.—Scans obtained in the anteroposterior projection on Case No. 26-47-81.

Fig. 3.—Scans obtained in the lateral projection on Case No. 26-55-47.

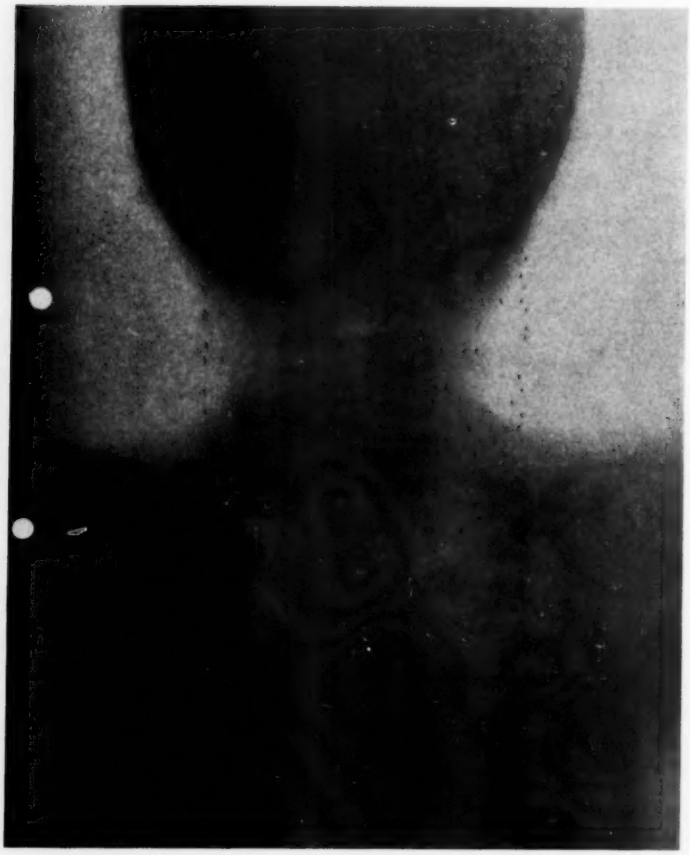


Fig. 4.—Scans obtained in the anteroposterior projection on Case No. 26-55-47.

week. Excretion is neglected as an added safety factor; 0.66 microcuries per pound body weight yields a satisfactory result with our scanner; however, up to 1.03 microcuries per pound may be employed.

The following two cases are presented for illustration:

REPORT OF CASES

CASE 1. N.C.B.H. (Unit No. 26-47-81). Six year old female was presented by her mother who noticed a growth at the base of the patient's tongue at age five. The mass was biopsied by her local physician and a histological diagnosis was inconclusive. The patient was entirely asymptomatic except for snoring. Family history, past history, and accessory clinical findings were unremarkable. Physical examination revealed a healthy six year old; height, 43 inches; weight, 44 pounds. The only remarkable finding was an irregular firm sessile mass 1.5 cm in diameter protruding at the base of the tongue below the vallate papillae. The mass was examined under anesthesia and no external drainage or duct was identified. Twenty-eight microcuries of radioactive iodine were administered, and the scan performed 24 hours later is seen in Figures 1 and 2. It is observed that the mass protruding into the pharyngeal air shadow at the base of the tongue, represents the entire thyroid of the patient.

CASE 2. N.C.B.H. (Unit No. 26-55-47). A four and one-half year old white female was presented, with a history of a growth at the base of the tongue, noted by her mother at age three. The patient was asymptomatic except for inability to swallow in the recumbent position. Family history, past history and accessory clinical findings were unremarkable. Physical examination revealed a healthy four and one half year old, weight 38 pounds, height 41 inches. The only remarkable finding was a bluish 2.5 x 1 cm mass at the base of the tongue which felt slightly cystic on palpation. No external drainage or duct was visualized. Twenty-five microcuries of I^{131} were administered and the patient scanned after 24 hours (Figs. 3 and 4). The thyroid in this case is in normal position and no uptake was obtained over the soft tissue mass at the base of the tongue.

COMMENT

The specific affinity of iodine for thyroid tissue makes radioisotope techniques as accurate as histologic techniques in its positive diagnosis. Scanography lacks the hazards of surgical biopsy and gives accessory information as to the entire distribution of thyroidal tissue. If the total thyroid gland is represented by the mass (as in Case 1), surgical biopsy is not necessary and probably contraindicated.

CONCLUSION

The application of scanographic techniques in the differential diagnosis of masses at the base of the tongue in children and in infants, we believe, is a safe and valuable technique.

WAKE FOREST COLLEGE

REFERENCES

1. Meschan, Isadore, and Taylor, C. Fred: Adaptation of Polaroid X-ray Paper Prints to Radioisotopic Scanner Techniques. In press.

VIII

THE TOO SMALL MOUTH IN PATIENTS WITH "PLUMMER-VINSON" SYNDROME

R. J. H. Kruisinga

AND

Eelco Huizinga

Groningen, Netherlands

The name "syndrome of Plummer-Vinson"[1] is now generally known. They were the first to draw attention to the connection between hypochromic anemia and dysphagia. Only, they considered this a functional disturbance, they spoke of "hysterical dysphagia." It is now certain that the explanation of this dysphagia often lies in an organic defect which can be the cause of the growth of cancer.

It is also often called sideropenic dysphagia. This name is not quite correct, as it only covers part of the patients. We are dealing here with a syndrome with a great many symptoms, some of which may be missing, as, for instance, dysphagia. Iron certainly plays a part in this syndrome. But at the moment it seems doubtful whether a shortage of iron is always responsible for all disturbances. We have seen many patients who had no anemia or a deficiency of iron in the blood serum. Other authors have also described this. Apparently anemia is not so essential a symptom with this syndrome as has been formerly assumed. On the other hand, the iron balance of these patients is said always to be disturbed. Anyway, it is certain that at the moment we are not completely informed about this interesting syndrome.

There is a remarkable difference in geographical spread, it occurs frequently in Holland and in the Scandinavian countries, and, it seems to us, more in the north of Holland than in the south.

The purpose of this article is to draw attention to a symptom which has from time to time been described in the literature without,

From the Oto-Laryngological Clinic of the University of Groningen.

Figure 1

Figure 2

however, becoming as well known as it deserves. This is the too small mouth, a striking feature in most patients, which in Holland was pointed out by Wassink.[2] Already many years ago we were struck by the characteristic appearance of patients with the Plummer-Vinson syndrome. Figure 1 is a typical example. It shows a woman of 49 years, a classic case of the Plummer-Vinson syndrome. In this age of laboratory research it is perhaps useful to draw attention again to symptoms which can be observed simply by inspection. It is therefore quite remarkable that in several handbooks a picture of a Plummer-Vinson patient is not to be found.

In order to find out the significance of the small mouth, all patients who visited the policlinic in the course of one year and who were suspected of Plummer-Vinson, were examined for this symptom. The starting point was always the dysphagia, which is logical in a laryngological clinic. Naturally, in another clinic a quite different grouping of symptoms will be found. Those women who visit the internist with general complaints, usually fatigue, nearly always suffer from hypochromic anemia. Here follows again an enumeration of the symptoms with this syndrome, all of which were examined: 1) dysphagia; 2) a too small mouth; 3) perlèche; 4) atrophy of the mucous membrane of the tongue and pharynx; 5) falling-out of the teeth (most patients get a prosthesis when still young); 6) falling-out of the hair (often the hair looks very untidy); 7) nail-defects;

8) fluor albus; 9) achylia which is refractory against histamine; 10) deficiency of iron in the blood serum.

With the help of the internal clinic (Prof. van Buchem) we made a careful investigation to see which of the symptoms mentioned above could be found. We only took patients (all were women) in whom at least seven symptoms were positive. All had dysphagia; as we have already mentioned, was this the complaint which caused them to come to us. During this year there were nine women with at least seven positive symptoms.

This investigation did not result in any new ideas on the genesis of the Plummer-Vinson. All these patients were examined on deficiencies of riboflavin, folium acid and vitamin B_{12}. The results were completely negative. The excretion of the 17-ketosteroids, gonadotrophin and estrogenous compounds also proved to be normal.

A very simple method was found to demonstrate that the mouths of these women really are too small. Figure 2 shows how with the help of two spatulae the mouth is drawn broadwise until it becomes uncomfortable for the patient; the distance is then read on a measuring-tape. It could be thought that the perlèche is the cause of the difference in measure between normal women and women with this syndrome. However, in ten women with perlèche but without this syndrome completely normal values were found.

In 94 normal women the average breadth of the mouth, measured as indicated on Figure 2, was 11 cm. In these nine women with the Plummer-Vinson syndrome the breadth was always considerably below average, e.g., respectively, 8, 8½, 8, 9, 9, 8¼, 8, 8¾ and 9¾ cm. Thus the characteristic appearance of this syndrome definitely includes the too small mouth. Often the diagnosis can be put fairly definitely already at first sight. These women often have a sad, asthenic face; striking is also the small mouth with perlèche, the false teeth and untidy hair. Typical examples are given on Figures 1 and 5. But this last woman had cancer of the mouth of the esophagus.

Of these nine patients, seven had perlèche, seven had smooth tongues and eight had defective nails, while in only two patients hypochromic anemia was found.

In five patients anomalies were found in the course of the x-ray examination and the esophagoscopy. With these patients the x-ray examination is difficult; the Waldenström[3] technique must be fol-

a. b.

Figure 3

lowed carefully. A viscous bariumpap is used, and the patient must swallow to order, which often causes difficulties. It is of the utmost importance that the photograph is taken at the right moment, as we express it: "the photo must be shot."

On these patients, as well as on many others, esophagoscopy was performed. We must admit that we have seen little of the "webs." On the other hand, many patients showed leucoplakia with easily bleeding rhagades, as has been first described in Holland by Gerlings.[4] There was often an obvious spasm. This was particularly noticeable in a woman of 35 with a typical syndrome and a very serious dysphagia, whom we saw a few years ago. In the mouth of the esophagus was leucoplakia with easily bleeding fissures. The reason for the dysphagia lay in a fixed stenosis, which during the first two esophagoscopies was thought to be a strongly fibrous scar-stenosis. With the first esophagoscopy this stenosis was with some trouble dilated to Ch.14 and with the second to Ch.22. With the third esophagoscopy the stenosis suddenly disappeared completely, so it was a spasm after all.

Interesting with these nine patients was the fact that among them were two identical twins of 43 years of age. This could be determined with certainty through examination of blood, sputum and

Figure 4

Figure 5

iris. These sisters did not have the typically sad and asthenic appearance of the Plummer-Vinson, as can be seen in Figures 3a and 3b. But again one is struck by: the too small mouth with perlèche, the prosthesis, the smooth tongue. It is interesting how the circumstances in life of these two sisters were quite different; one was a farmer's wife, while the other was the wife of a skipper. The first woman came to the clinic because she was suddenly unable to swallow. She had swallowed a cherry-stone which had got stuck in the mouth of the esophagus and had to be removed by esophagoscopy, again the spasm.

It is often assumed that there is a relation between Plummer-Vinson and carcinoma of the mouth of the esophagus. In Holland Wassink has also drawn attention to this. When one has often performed esophagoscopy on patients with Plummer-Vinson and has seen the leucoplakia and the easily bleeding rhagades, one does not wonder that several of these women get carcinoma later on.

In the different countries there is a considerable difference in statistics about carcinoma, where the percentage of women is concerned. This can probably be explained by this connection. In countries where Plummer-Vinson frequently occurs, we also find relatively many women with carcinoma of the esophagus. Esophagus-carcinoma is really a disease of elderly men. But in a number of

TABLE I

CANCER OF THE ESOPHAGUS

MEN 220 WOMEN 80

		UPPER THIRD	MIDDLE + LOWER THIRD	CARDIA
Men	51 years and more	203	17	100	86
Women	51 years and more	52	16	22	14
Men	50 years and less	17	5	6	6
Women	50 years and less	29	16	8	4

countries a considerable percentage is formed by women. The average age of these women is much younger and the localization of the carcinoma is almost high. This appears also from our statistics.

In Holland Plummer-Vinson as well as high carcinoma of the esophagus occur frequently in women. We have considered carcinoma of the mouth of the esophagus and postcricoid carcinoma as belonging to one group. In practice it is usually hard to distinguish between these two.

With carcinoma of the esophagus it is usual to distinguish between the following four localizations: high, middle, low, cardia. Cardia-carcinoma is nearly always an adenocarcinoma, and in reality a gastric carcinoma, which has grown into the esophagus. Table I shows the statistics of a continuous series of 300 patients who definitely had cancer of the esophagus; in all these cases the biopsy was positive.

For 220 men we find no less than 80 women, that is a relation of less than three to one. This is very different from many statistics, where the relation is often found to be ten to one.

It has also struck us how these women with a high localization of carcinoma often have a long previous history of difficulties with swallowing, while again and again we noticed that these women so often had the same appearance as those with the syndrome of Plummer-Vinson. Here follows a typical example.

Figure 4 shows the photograph of a woman of 55 with cancer of the mouth of the esophagus and the postcricoid region. We had seen here ten years previously with a dysphagia, which she had then

been complaining about for a long time. She had a very characteristic Plummer-Vinson syndrome with hypochromic anemia. She had to be dilated for the spasm of the mouth of the esophagus and she was treated in the usual way with large quantities of iron. The therapy was soon completely successful, but against our advice she did not return for a check-up. Ten years later we saw her again with carcinoma.

When one takes a thorough anamnesis of these women with cancer of the esophagus, one repeatedly finds: complaints about swallowing for a long time. Figure 5 is a photograph of a woman of 48 with cancer of this location. It is a classic example of the Plummer-Vinson syndrome, nearly all the symptoms were there. Noticeable is again the sad asthenic appearance with the untidy hair. The mouth is obviously too small and she wears a prosthesis. All her life she had had trouble swallowing, increasingly so in recent months. She indicated that she had always been troubled by too narrow a gullet. This complaint is often heard spontaneously from these patients. When we observe again the very small mouth on the photograph of Figure 5 and think of her complaint and the anomalies which are objectively found in these patients, then it could indeed be possible that the proportions of the mouth of the esophagus are abnormally narrow. But if this really is the case, then this cannot be so easily expressed in measurements, as was done for the mouths of these patients.

SUMMARY

Attention is drawn to a little known symptom of the Plummer-Vinson syndrome. The mouths of these women are often too small. A method is described to express this in measurements. This same anomaly is also often found in women with high localization of cancer of the esophagus. Statistics of carcinoma of the esophagus in Groningen are discussed. It is assumed that there must be a relation between the Plummer-Vinson syndrome and the high localization of carcinoma in women. Once more the typical appearance of many of these patients is pointed out.

ACADEMISCH ZIEKENHUIS

REFERENCES

1. Vinson, P. P.: Minnesota Med. 5:107, 1922.
2. Wassink, W. F.: Ned. Tijdschr. v. Geneeskunde 79:1491, 1935.
3. Waldenström, Kjellberg and Roland: Acta Radiologica 20:618, 1939.
4. Gerlings, P. G.: J. Laryngol. and Otol. 55:149, 1940.

IX

CHEMICAL BURNS OF THE MOUTH, PHARYNX AND ESOPHAGUS

Bobby R. Alford, M.D.

Herbert H. Harris, M.D.

Houston, Texas

A distressingly perplexing problem is often presented by the patient who has ingested a corrosive substance. The over-all incidence of this problem may have been reduced as a result of legislation instigated by Chevalier Jackson in 1927; however, it is still a frequent problem in our area of the United States, where alkali and phenol are used by the low economic group to make soap, clean or disinfect. The problem is not confined to the United States and must be a universal one, because papers on this subject have been reported from Russia,[25] South Africa,[15] India,[1] Formosa,[14] Singapore,[18] Yugoslavia,[11] and other countries.

In the twelve years between 1946 and 1958, 118 patients were admitted to Jefferson Davis Hospital with chemical burns of the mouth, pharynx, or esophagus (Table I). Seventy-nine of these patients were in the pediatric age group. These patients were admitted to the pediatric service and managed jointly from the beginning by that service and the otolaryngology service. In recent years it has been the policy for the otolaryngology and general surgery services to work together with respect to the long-term management of these problems.

ANALYSIS OF CASES

Alkali burns accounted for 96 of the 108 cases. As noted above, 79 patients were less than 14 years of age. Twelve patients had burns caused by acids, usually phenol, but in two instances, hydrochloric acid. Acid ingestion resulted in only two esophageal burns,

---

Presented before the monthly meeting of general pediatric Staff, Texas Children's Hospital, March 17, 1958, and Otolaryngologic Staff Meeting, April 14, 1958.

From the Department of Otolaryngology, Baylor University College of Medicine, and the Jefferson Davis Hospital, Houston, Texas.

both at the cricopharyngeus; however, neither of these patients developed strictures. There were no deaths caused by acid ingestion, and only one patient manifested systemic phenol effects.

Thirty-two of the 96 patients with alkali burns had esophageal burns (Table II). Fifteen of these had burns at the cricopharyngeus, 10 had burns in the middle third of the esophagus in the region of the aorta, or left main stem bronchus, 11 patients had burns at the cardia, and 6 patients had diffuse esophageal burns (Table III). There

TABLE I

CHEMICAL BURNS OF MOUTH, PHARYNX AND ESOPHAGUS
JEFFERSON DAVIS HOSPITAL
1946 - 1958

Alkali Burns	96
Acid Burns	12
Total	108

TABLE II

ALKALI BURNS (96 Cases)

Number with Esophageal Burns	32
Number Forming Strictures	17
Number Deaths	5

seemed to be very little relationship between the burns in the mouth and the presence of esophageal burns, except that every patient with an esophageal burn had burns somewhere in the mouth or pharynx. No relationship existed between these patients with esophageal burns and the form of alkali ingested; all forms (crystal, powder and liquid) caused burns of the esophagus.

With respect to the relationship between oropharyngeal burns and esophageal burns, it is important to note that seven patients with esophageal burns had no evidence of posterior pharyngeal burn. Five patients with esophageal burns had no evidence of damage to the anterior pillars, or pharynx.

Seventeen patients who ingested alkali formed strictures of the esophagus requiring treatment. The most common place for stricture formation in our group of patients was the middle third of the esophagus, where six patients formed strictures. Four patients formed multiple strictures. Four patients had strictures at the cricopharyngeus and three patients had strictures at the cardia (Table IV).

Spontaneous esophageal perforations occurred in two patients, one of these resulting in death. One patient perforated at the anastomotic site of esophagogastrostomy and subsequently died.

We have managed satisfactorily with dilatation 11 of the 17 patients with strictures. None of these 11 patients require dilatation at the writing of this paper, but are given clinic follow-up visits for re-evaluation.

Operative procedures have been performed on six patients with esophageal strictures, all refractory to dilatation (Table V). Four patients had esophagogastrostomies, one had a segmental esophagectomy and one patient has had an antethoracic ileocolic transplant.

TABLE III

LOCATION ALKALI BURN

Cricopharyngeus	15
Middle Third	10
Cardia	11
Diffuse	6

TABLE IV

LOCATION OF STRICTURES

Cricopharyngeus	4
Middle Third	6
Cardia	3
Multiple	4

There have been five deaths caused by alkali ingestion (Table VI). Two patients died within 48 hours of perforation of the esophagus or an abdominal viscus and aspiration. One patient died after 11 days as a result of aspiration pneumonia. One died as a consequence of esophageal perforation at dilatation; and one died as a result of perforation at the site of esophagogastrostomy.

COMMENT

Certainly more rigid controls over the availability of these agents should be strived for, because most of the patients who ingest them are much too young to realize the dangers. Also, it seems unnecessary for this problem to arise in view of the safe inexpensive soaps, cleaners, and disinfectants available today.

The pathological changes incurred by the acid and alkali are well reviewed by Burford.[3] The coagulative necrosis with increased inflammatory reactions caused by acids probably accounts for the apparent limitation of damage by them; the result is fewer strictures. This is well-corroborated by the 12 patients in this series who ingested acid. In contrast, the liquefactive necrosis caused by alkali agents definitely has untoward effects.

As noted in the analysis of cases, 33 per cent of our patients who ingested alkali had esophageal burns; over 50 per cent of these

resulted in strictures requiring treatment. This agrees well with the incidence of stricture formation reported by Hands,[13] and Marchand[16] and with the incidence of burns of the esophagus reported by Gusic.[11]

The previous percentages point out the practical importance of endoscopy in determining whether or not an esophageal burn exists. Economically, it is important to determine early if any treatment of the esophagus will be required. Davis[9] examines the patient endoscopically in 48 hours, Marchand[16] one week, Cody[5] in four to five days,

TABLE V

OPERATIVE PROCEDURES PERFORMED

Esophagogastrostomy	4
Segmental Esophagectomy	1
Antethoracic Ileocolic Transplant	1

TABLE VI

CAUSE OF DEATH

Immediate Perforation of Esophagus and Aspiration	2
Aspiration Pneumonia	1
Perforated Esophagus Secondary to Dilation	1
Perforation Site of Esophagogastrostomy	1

Brophy[2] in three to ten days, Hands[13] in two or three weeks, Daly[7] in the first two weeks, Burford[3] in three weeks, and Buckman[4] in four weeks. It is pertinent to point out that we have performed diagnostic esophagoscopies on 69 patients within the first two weeks. None of these patients had complications due to endoscopic examination, and no burns were missed by the endoscopist.

Candidates for surgical reconstruction include those patients with complete stenosis without a lumen, those patients with marked irregularity, or fistula formation, those patients who cannot be dilated because of complications secondary to dilatation and strictures that cannot be kept open by dilatation. These criteria agree with those of Daly,[8] Finnerty,[10] and Hanckel.[12]

Thirty-five per cent of our patients with strictures have been unsuccessfully treated by conservative management and have required surgical reconstruction. This is in close accordance with the experience of Marchand,[17] who reports that 41 per cent of his patients have to be operated upon. For the largest number of operated cases with strictures, the reader is referred to Petrov,[19] who with Yudin's[25] cases, has had experience with 634 patients subjected to esophageal reconstruction.

Many types of operative procedures have been suggested, however, one must recognize that surgical reconstruction also has its problems. This is particularly exemplified in our group of operated cases where it has been noted that esophagogastrostomy has the problem of anatomic limitation and stenosis at the anastomotic site, requiring revision, or dilatation postoperatively. Jejunal and ileocolic transplants are complicated by stricture formation at anastomotic sites and occasional infarction of the transplant due to insufficient blood supply. Quite frequently it is difficult, hazardous, and unjustified to remove the burned esophagus. Also, it is difficult at times to be sure the anastomosis is above the extent of the stricture.

In recent years adrenal steroids have been used by many. We used steroids in only four patients, none of whom when examined had esophageal damage. Obviously this small group of patients has little meaning. For additional information about the experimental and clinical use of these agents, the reader is referred to papers by Pfundt,[20] Weisskopf,[24] Rayes,[21] Rosenberg,[22] Dagradi,[6] and Smith.[23]

Certainly, when presented a patient who has ingested one of these chemicals, we believe that the best management is accomplished by a combined approach to the problem by the otolaryngologist and the surgeon. However, it is to be understood that the best treatment for ingestion of corrosive chemicals is neither dilatation nor surgical reconstruction, but absolute prevention.

SUMMARY

1. Chemical burns of the mouth, pharynx and esophagus are relatively frequent problems in our area of the United States.

2. One hundred and eight patients with chemical burns of the mouth, pharynx, or esophagus were studied. Twelve patients ingested acids without stricture formations, or death. Ninety-six patients ingested alkali. Thirty-two patients ingesting alkali had esophageal burn, and seventeen of these developed strictures. Five deaths due to alkali ingestion occurred.

3. There is very little relationship between esophageal damage and the form of ingested chemical, or extent of oral burn.

4. Esophagoscopy early is a safe, practical way to determine the extent of the burn.

5. Strictures of the esophagus formed most frequently in the middle third.

6. The majority of patients with strictures can be managed by dilatation. Thirty-five per cent require surgical reconstruction.

7. A combined approach to the problem by the otolaryngologist and general surgeon is the best practical management today.

907 HERMANN PROFESSIONAL BUILDING

REFERENCES

1. Betts, R. H., and Thomas, T.: Cervical Esophagojejunostomy for Extensive Stricture of the Esophagus. Surgery 38:553, 1955.

2. Brophy, J. W.: Esophageal Strictures Following Ingestion of Caustic. Stanford Medical Bulletin 14:230, 1956.

3. Burford, T. H., Webb, W. R., and Ackerman, L.: Caustic Burns and Their Surgical Management. Ann. Surg. 138:453, 1953.

4. Buckman, J. A., and Gay, E.: Surgical Treatment of Extensive Lye Strictures in Children. Amer. Surgeon 21:370, 1955.

5. Cody, III, C. C.: Recent Trends in Management of Esophageal Strictures. ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY 63:1120, 1954.

6. Dagradi, A. E., and Stempein, S. J.: Cortisone, Corticotropin and Procaine in Treatment of Corrosive Esophagitis. S. J. Calif. Med. 81:33, 1954.

7. Daly, J. F.: Early Management of Corrosive Burns. S. Clin. N. A. 34:343, 1954.

8. Daly, J. F., and Cardore, J. D.: Corrosive Esophagitis. Amer. J. Surg. 93: 242, 1957.

9. Davis, M. V.: Early and Late Management of Caustic Burns of the Esophagus. Amer. Surgeon 22:308, 1956.

10. Finnerty, J. J.: Late Treatment of Caustic Strictures. S. Clin. N. Amer. 34:353, 1954.

11. Gusic, B.: Changes in Blood Vessels and Nerves of Esophagus Due to Corrosion by Ingested Caustic. J. Laryngol. and Otol. 67:745, 1953.

12. Hanckel, R. W.: Lye Burns of the Esophagus. ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY 60:22, 1951.

13. Hands, J. C., Jr.: Caustic Burns of the Esophagus; A Ten Year Analysis. Amer. J. Surg. 91:742, 1956.

14. Hung, W. C., Huong, S. A., and Lai, C. T.: Lye Burns. A.M.A. Arch. Otol. 57:282, 1953.

15. Marchand, P.: Caustic Soda Poisoning. Sociological Aspects. South Africa J. Med. 38:415, 1954.

16. Marchand, P., Fatti, L., and Crawshaw, G. R.: The Treatment of Caustic Strictures of the Esophagus. S. G. O. 10:195, 1956.

17. Marchand, P.: Caustic Strictures of Esophagus. Thorax 10:171, 1955.

18. Mekie, E. C.: Simple Stricture. Brit. J. Surg. 42:39, 1954.

19. Petrov, B. A., Addendum, Betts, R. H.: Cervical Esophagojejunostomy for Extensive Stricture of the Esophagus. Surgery 38:553, 1955.

20. Pfundt, T. R.: The Prevention of Esophageal Stenosis from Alkali Burns in Children. J. Okla. State Med. Assn. 49:521, 1956.

21. Rayes, Morgan: Cortisone Treatment of Lye Burns of the Esophagus. J. Pediat. 49:394, 1956.

22. Rosenberg, N., Kunderman, P. J., Vroman, L., and Moulten, S. E.: Prevention of Experimental Lye Stricture of the Esophagus by Cortisone. A.M.A. Arch. Surg. 63:147, 1951.

23. Smith, V. M., and Compton, J. R.: Cortisone and Acute Lye Corrosion. Otolaryngol. 58:235, 1953.

24. Weisskopf, A.: Effects of Cortisone on Experimental Lye Burn. ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY 61:681, 1952.

25. Yudin, S. S.: The Surgical Construction of 80 Cases of Artificial Esophagus. S. G. O. 78:561, 1944.

X

ELECTRONYSTAGMOGRAPHIC STUDIES OF VESTIBULAR FUNCTION

METHOD AND PROCEDURE

GODFREY E. ARNOLD, M.D.
VITO GIULIANI, M.D.
AND
GEORGE STEPHENS, M.D.
NEW YORK, N. Y.

PRINCIPLES OF OBJECTIVE NYSTAGMOGRAPHY

All recent investigators agree that the accepted methods of clinical vestibular tests are rather unreliable. Almost each examiner is accustomed to his individual standards of rotatory and particularly of caloric testing. Thus, the results of different clinics cannot be directly compared. The source of greatest error stems from the fact that nystagmus is customarily observed in a subjective manner. Again, all authors agree that it is very difficult to watch at the same time for the various characteristics of nystactic movements and to describe their magnitudes in semantic terms. Moreover, the fine details of all ocular movements, such as their precise onset, frequency, amplitude, regularity, duration, and termination, cannot be adequately recognized by the naked eye. Unless a permanent graphic record of all details of the entire nystagmus pattern is obtained, no objective and exact comparison of different test results can be attempted. Many authors experimented with such objective methods. For the purpose of a survey one may distinguish procedures with mechanical, optical, photographic, photoelectric, and electrographic principles.

1. Around the turn of this century mechanical and optical systems were tried. Dewar[6] or LeHeux and DeKleyn[17] accomplished a graphic record by connecting writing rods to the anesthetized cornea. Eye movements were then transcribed on a moving paper strip. A

From the Department of Research, New York Eye and Ear Infirmary. This study was aided by the John Hartford Foundation.

manometric system connected to a rubber cup placed over the eye was used by Ohm.[31] Kuilman[16] continues to employ an optomechanical principle. It is valuable for the demonstration of rotatory nystagmus.

2. Photographic methods attracted much interest, such as the attachment of small mirrors over the closed eyelids which reflected a light beam on a continuously moving film.[46] Similar principles were employed by numerous other investigators (Linthicum, Struycken, etc.). For practical purposes it is time consuming to await the photographic development of the film.

3. Photoelectric methods. Van Gemert and Duyff[45] placed a contact glass on the eye. It was connected to the mobile plate of a parallel-plate air capacitor. Rotation of the contact glass as a result of horizontal nystagmus causes a capacity change in the capacitor. This is part of a high frequency voltage divider, the output of which is rectified, amplified, oscilloscopically recorded, and filmed. Due to the direct connection between the contact glass and the eye, these authors claim a strictly linear relationship between the oscilloscopic spot deflection and the degree of eye rotation. Hence, this type of nystagmogram is said to present a direct and immediate record of actual eye movements without the need of further differentiation. A practical disadvantage is the difficulty in applying and handling contact glasses, which may also modify the eye movements.

Torok, Guillemin and Barnothy[43] utilized a photoelectric cell to record variations in the reflection of an infra-red light beam focused on the corneoscleral margin in such a way that it falls partly on the sclera and partly on the iris. As a result of nystactic eye movements, the portion of the light beam reflected from the sclera increases and decreases at the rhythm of the nystagmus. The proportional changes in reflected brightness produce a photo-electrically generated current which is amplified and actuates a direct pen writing recorder. Again, this photo-electric nystagmogram reveals the eye movements directly and accurately. The photo-electric registration by Pfaltz and Richter[33] employed two photo-electric cells for the recording of homogeneous illumination of the moving eyes. All these methods share the disadvantage that the eyes must be kept open. The blinking reflex interferes with the continuity of the record.

4. Electrographic methods of recent times permitted the development of objective nystagmography to its present stage.[32] An account of various attempts in this direction was given by Torok, Guillemin and Barnothy.[43] They also quoted the bibliographic survey by Marg.[20] The physiologic basis of electric nystagmography

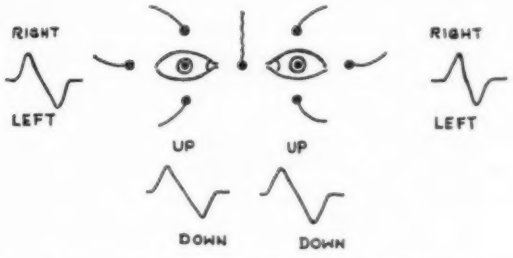


Fig. 1.—Placement of electrodes for vertical and horizontal registration of nystagmus and code for polarity arrangement according to Bergman.

(ENG) is the recording of changes of the constant corneoretinal potential, particularly of its standing potential, in fixed skin electrodes placed around the eye. This corneo-retinal potential was discovered by DuBois-Reymond in 1849 and thoroughly investigated and defined by Mowrer in 1936.[30] Since the posterior part of the eye with the retina is electro-negative, and since the anterior segment with the cornea is electro-positive, all movements of the eye will cause a change of this potential in relation to suitably placed electrodes. This is known as the Mowrer principle. A detailed account of its theory and some mathematical evaluations were presented by Marg in 1951.

It is important to remember that the graphic records must be interpreted according to the type of amplifiers used. With a direct

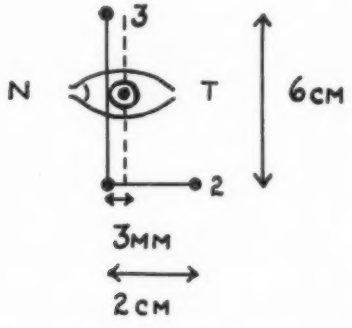


Fig. 2.—Another method of electrode placement. N=nasal, T=temporal, 1-2: horizontal lead, 1-3: vertical lead. Note suitable distances.

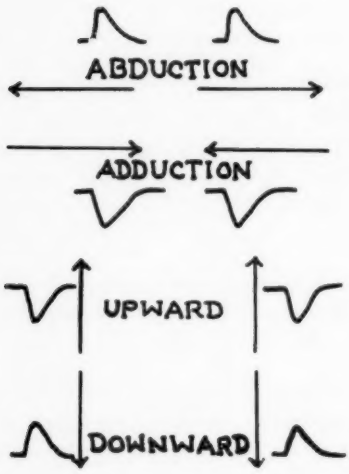


Fig. 3.—Code of polarity adjustment and interpretation of electrical deflections according to Montandon.

current amplifier, the change in the voltage recorded through the electrodes is proportional to the angle displacement of the eye.[32] With an alternating current amplifier, or in case of a capacitative connection between leads and amplifier, the nystagmographic curve contains a differentiated translation of several modalities of the eye movements: direction, angular deflection, frequency, and acceleration. For this reason the graphic record gives no information on the stationary location of the eye. The slope of each individual deflection corresponds to the acceleration of the ocular movement. The amplitude of the graphic deflection represents rather the velocity of the eye

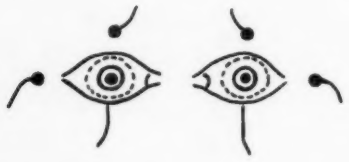


Fig. 4.—Arrangement of contact glass electrodes according to J. Jacobson. Polarities may be adjusted as desired.

movement. In this manner a sharp rise from the base line indicates a rapid change in position, whereas a gradual rise represents a positional change with slow acceleration. A high amplitude means a rapid eye movement, while a low amplitude signifies a movement of slow velocity.[4] Therefore, the ENG must not be misconstrued to depict the actual pattern of the eye movements. The pen will return to its base line, even though the eye remains in an abducted position. It remains a problem of standardized, calibrated, and integrated recording to correlate the nystagmogram with the clinically important modalities of nystactic eye movements.

While the first electronystagmographic recordings were achieved with EKG equipment,[12,21,22,38] present investigators prefer the standard instruments for EEG. In spite of diligent work in many institutions, no general agreement on a standardized procedure has yet been reached so that the electronystagmograph remains an experimental tool for the time being. This is one of the reasons for the continuous elaboration of other means of electrographic recording.

Modifications of nystagmographic procedure were suggested by several other authors. Henrikson[9,10] demonstrated how the speed of the slow nystactic phase can be read directly from the amplitude of the ENG curve. A precise measurement of the threshold values for the various phases of rotatory nystagmus was achieved by Montandon:[24-29] $1°/sec^2$ for deceleration nystagmus. Stahle[39] described average normal values for the caloric ENG. Detailed accounts of technical problems were discussed by Pivotti and Lucarelli.[34,35] According to Reich,[36] a differentiation between central, vestibular, and ocular nystagmus may be achieved by the simultaneous registration with the time constants used for EEG, EKG and EMG.

Mahoney, Harlan and Bickford[19] concurred with Dieterle and Monnier[7] in stressing the variability of routine caloric test results, because they depend on many physiologic factors. They employed the technique of ENG for a study of such modifying factors. In addition to the general criteria of vestibular response, namely, 1) latency, 2) amplitude, 3) frequency, and 4) duration, these authors consider the graphic record valuable for two further qualities of nystagmus pattern: 5) amplitude stability and 6) frequency stability. Observations were made regarding the effect of fixation, vision, eye closure, and mental activity on caloric nystagmus. As the influence of fixation was reduced, the rate of the nystagmus decreased, while its amplitude increased. Parallel with this change, the frequency and amplitude stabilities appeared diminished. Similar observ-

ations were reported by Aso,[3] Kirsten and Schoepfer,[14] Aschan and Bergstedt,[2,14] as well as Montandon and Russbach.[20] Further details of the findings by Mahoney[19] and collaborators are summarized in Table I.

TABLE I

AVERAGE AMPLITUDE, FREQUENCY, AND DURATION OF CALORIC NYSTAGMUS RECORDED

	AMPLITUDE (degrees)	FREQUENCY (seconds)	DURATION (seconds)
Fixation at 30 cm (18 subjects)	3.3	3.1	102
Eyes gazing into infinity (14 subjects)	6.0	2.3	119
Frenzel glasses (16 subjects)	12.0	2.2	132
Eyes open in dark (16 subjects)	13.0	2.2	155
Eyes closed (18 subjects)	19.0	1.9	184

PROCEDURE OF ELECTRONYSTAGMOGRAPHY

In agreement with Bergmann, Nathanson and Bender,[4] Montandon, Monnier and Russbach,[28] Mahoney, Harlan and Bickford[19] and other authors, we feel that the most practical method for further advances in electronystagmography is the use of standardized equipment readily available in larger hospitals. This is the electroencephalograph. At present, we are working with the Grass Model III D. It records graphic curves with controllable paper speed. It was found that among several available time constants (EKG=0.3, EEG=0.1), the EMG time constant of 0.05 with a paper speed of 1.5 to 3 cm per second was most advantageous for our purposes. Suitable filters were used for the elimination of distracting potential changes of higher frequencies generated elsewhere in the body. Generally, a calibration of 100μV with an amplication of five times was found practical in all recordings channels.

Electrodes are standard silver plates with a diameter of one quarter inch. These are fixed to the skin by means of EKG jelly and black electrical tape. The position of the electrodes around the patient's eyes varies according to the specific purpose of recording. Bergman, Nathanson and Bender[4] recommended the following arrangement: one electrode above, and one below each eye, one lateral to each outer canthus, and one on the bridge of the nose (Fig. 1). In this manner, the superior-inferior electrode pairs record vertical movements and

are connected through channels 1 and 2 of the electroencephalograph, while the temporal-nasal electrodes through channels 3 and 4 record the horizontal movements. The polarities are adjusted in such a way that upward movements of the eyes are recorded as upward deflections of the recording pens and downward movements as downward deflections. In the horizontal recordings, a movement to the right produces an upward deflection of the pens, and a movement to the left results in a downward deflection.

Montandon, Monnier and Russbach[28] specified another arrangement with constant distances between the electrodes. They selected a vertical lead from the superior and inferior orbital margins, with a maximal distance of 6 cm between the electrodes, and an axis 3 to 4 mm medially to the center of the pupil. For the horizontal lead, the lower electrode of the vertical pair was used together with a third electrode, placed 2 cm laterally from the former, along the inferior edge of the orbit (Fig. 2). These authors also suggested a convention on the polarity of the electrode connection in the following manner: abduction of the eyeball results in upward electro-negative ENG deflection; adduction (convergence) produces downward electro-positive deflection; upward gaze is expressed by downward electro-positive deflection; and downward gaze corresponds to upward electro-negative deflection of the ENG curve (Fig. 3). As can be seen, this arrangement yields inverted results as compared with the statements of the previous paragraph.

Apart from these external applications, the principle of contact glass electrodes may also be used. We tried in several cases to apply the contact lenses type KARP, modified by J. Jacobson. In addition to the contact lens electrodes, one then needs only a second electrode at the external canthus and a third electrode at the center of the upper orbital border of each eye (Fig. 4). However, contact electrodes have two disadvantages. One, they are disturbing to the subject and may cause minor irritations of the cornea with consequent displeasure of the patient. Two, any foreign body applied directly over the eye may interfere with the fine details of nystactic movements, thus introducing an extraneous artefact into graphic recording.

COMMENT

In the course of initial pilot study, we tried to gain experiences with the various methods and procedures recommended by previous authors. We selected a random group of patients with ear complaints from our clinics, and tested their vestibular function by administer-

TABLE II

CAMPARISON BETWEEN ENG RECORD AND SUBJECTIVE OBSERVATION

CASE, AGE	STIMULUS: CC ICE WATER	LATENCY: SEC. ENG	LATENCY: SEC. SUBJ:	DEGREE ENG	DEGREE SUBJ:	FREQUENCY PER SEC.	DURATION: SEC. ENG	DURATION: SEC. SUBJ:
1. O.S. 55 Meniere	AD 2	70	30	3	2	1	62	40
	AS 2	10	20	3	3	3	200	90
4. L.S. 59 Meniere	AD 2	20	20	3	2	2	160	100
	AS 2	30	20	1	2	2-3	130	90
5. V.T. 36 Meniere	AD 2	40	60	3	1	2	450	80
	AS 2	10	60	3	1	1	220	70
6. N.C. 43 Meniere	AD 2	120	30	1	1	0.5	110	60
	AS 2	15	20	3	3	1	140	100
9. D.A. 34 Meniere	AD 2	20	20	2	2	2-3	150	160
	AS 2	20	35	2	2	1	150	85
10. I.S. 35 Percept. loss	AD 2	25	20	2	2	1	125	60
	AS 2	35	20	2	2	1	100	60
11. R.P. 60 Meniere	AD 2	30	35	3	2	1	210	50
	AS 2	—	—	—	—	—	—	—
	AS 5	30	25	3	2	1	180	95
12. D.F. 47 Meniere	AD 2	20	30	3	3	3	180	140
	AS 2	—	—	—	—	—	—	—
	AS 10	15	30	2	2	3-4	240	120
13. M.K. 48 Central Hypacusis	AD 2	15	15	3	3	1-2	250	190
	AS 2	20	30	3	3	1-2	180	130
14. M.K. 48 Central Hypacusis	AD 2	15	15	3	3	1-2	250	180
	AS 2	15	30	3	3	1-2	350	180
15. D.M. 40 Meniere	AD 5	45	90	1	1	0.5	30	5-10
	AD 10	20	42	1	1	1	140	15
	AS 5	25	60	1	1	1	45	10
16. F.P. 74 Presbyacusis	AD 10	—	—	—	—	—	—	—
	AS 5	30	20	1	3	2	120	70
17. G.McN. 38 Percept. loss	AD 10	35	45	1	1	1	65	48
	AS 10	60	—	2	—	1	40	—
18. C.I. 29 Percept. loss	AD 10	45	45	1	1	1	60	40
	AS 10	35	—	1	—	1	35	—
19. L.P. 34 Conduct. loss	AD 2	30	30	3	2	1	90	95
	AS 2	35	40	3	2	1	120	100
20. E.C. 43 Percept. loss	AD 2	15	20	3	2	3	160	85
	AS 5	30	20	2	2	2	140	105

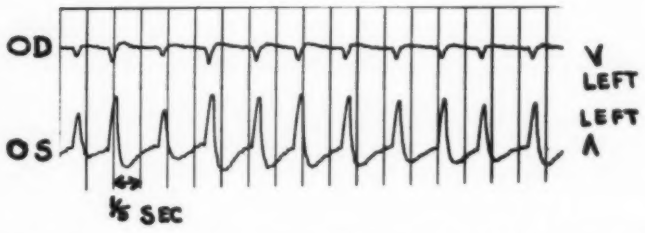


Fig. 5.—Electronystagmogram (ENG) recorded with contact glass electrodes and time constant for electromyography (EMG=0.05). Note polarities, direction of eye movements, and frequency per second. Case 12: 39 sec after stimulation of AD, normal response.

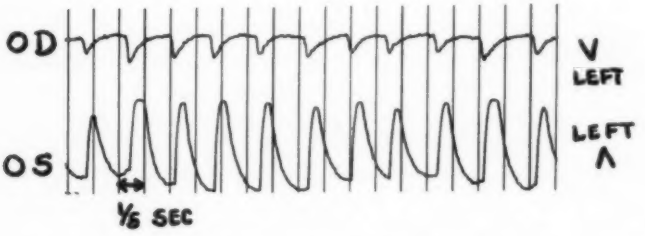


Fig. 6.—ENG recorded with contact glass electrodes and time constant for electroencephalography (EEG=0.1). Same (Case 12) at the same moment as in Figure 5.

ing the caloric test in the customary manner of this institution. During a first test, the vestibular reaction was observed subjectively, while at a later hour the same test was repeated with ENG recording. Frequently, both the subjective observation and the graphic recording were done concurrently. No particular emphasis was placed on a minute definition of all qualities of the test stimulus at that time. However, a gross comparison between the subjective visual observation of caloric nystagmus and the ENG recording of eye movements demonstrated promptly the frequently reported superiority of objective nystagmography.

Some of our findings are summarized in Table II. It can be seen that the magnitude of a vestibular reaction corresponds to the values of its latency, total duration, frequency, degree and amplitude.[22]

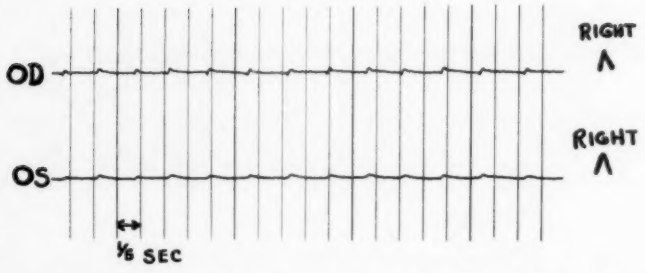


Fig. 7.—ENG recorded with skin electrodes (comp. with Figure 1). Case 1, 68 sec after stimulation of AS.

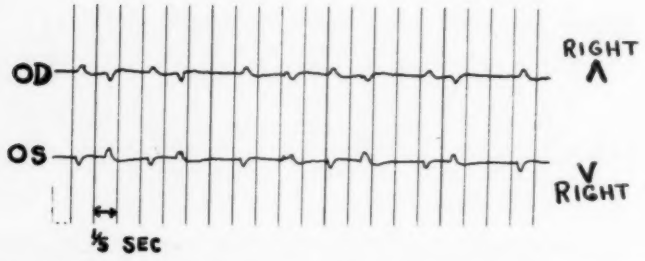


Fig. 8.—Bipolarity of nystactic beats. Case 4, weak response with nystagmus of I. degree, 40 sec after stimulation of AS.

However, we did not mention the amplitude values, because they require a precise calibration of the recording equipment and systematic calculation of the curves. This will be discussed at a later date. With regard to the recording technique, we made the following observations.

At first we tested with contact glass electrodes. They produce curves with large amplitudes which are easy to count. Figures 5, 6 and 7 illustrate the differences of records obtained with and without contact glass electrodes. As stated before, this procedure is unpleasant for the patient and may produce an inhibiting influence on the fine details of nystactic eye movements. Therefore, we do not recommend the use of contact lenses except for special purposes.

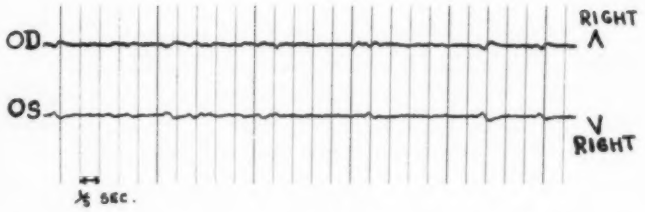


Fig. 9.—Nystagmus intensity at midpoint of its duration. Case 10, weak response with nystagmus of II. degree, one beat per second, 49 to 54 sec after stimulation of AS.

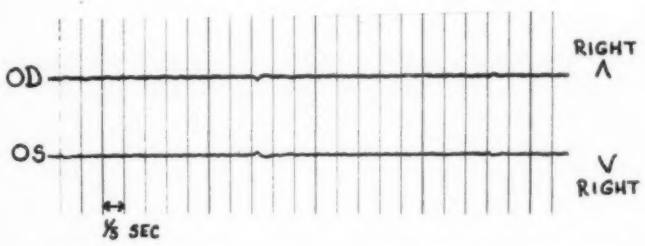


Fig. 10.—Nystagmus intensity at the end of reaction. Same case as in Figure 9. Nystagmus of II. degree, one beat in 2 sec, 91 to 95 sec after stimulation of AS.

It is a matter of general agreement that ENG shows many fine details of nystagmus which escape the observation of the naked eye. All time values are defined with great precision and differ again from the rather crude estimates by subjective inspection. In general, the latent time between the end of stimulation and the onset of nystagmus is much shorter on the ENG record. The duration of the nystagmus appears much longer, partly because of the shortened latency, and partly because the decaying end stage of nystagmus escapes the mere visual detection. Often, a higher degree of nystagmus may be noted on the ENG chart, while the unaided eye saw only nystagmus of first or second degree. Frequency cannot be determined precisely, except by actual counting of the recorded beats per time interval. Lastly, the amplitude of the eye movements as interpreted from the graph, presents the most important criterion of vestibular reaction. All these

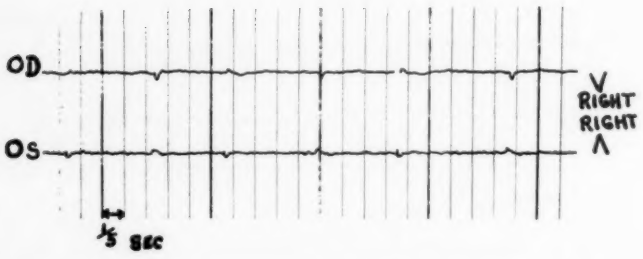


Fig. 11.—Pendulous nystagmus at the end of reaction. Case 15, reduced response with weak nystagmus of I. degree and five beats in 4 sec, 37 to 40 sec after stimulation of AS.

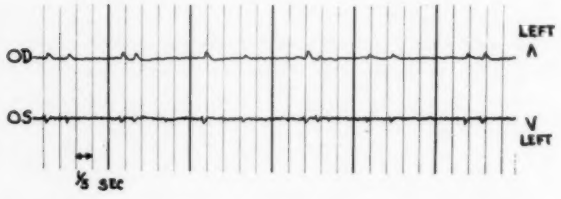


Fig. 12.—Dicrotic nystagmus during first third of a normal vestibular reaction time. Case 20, nystagmus II. degree, double nystactic beats at the rate of one per second, 47 sec after stimulation of AD.

factors are easily confirmed. In addition to these constant physiologic observations, we were confronted by several peculiarities.

In several cases (4, 12, 18, and 19) we found a bipolarity of the nystactic beats. Figure 8 shows first a positive deflection, corresponding to an eye movement in the direction of the expected quick component of the nystagmus. Shortly later, namely 0.2 to 0.4 sec, a second beat in the opposite direction is marked by the deflection with negative (or inverted) polarity. It is possible that this second eye movement is related to the slow component of the nystagmus. Such phenomena are now being investigated.

One of the major advantages of ENG is the accuracy in the determination of the gradually subsiding vestibular reaction. As is

well known to every clinical observer, the initially strong nystagmus decreases with a certain decrement. However, little information is available with regard to the precise values of the time-intensity relation of these variable decrements. Figures 9 and 10 illustrate the relative magnitudes of the subsiding reactions at two different moments. It is merely a matter of time to calculate the modality of the nystagmus beats and to correlate them with the course of the caloric reaction. Such calculation produces the decrement curve for each case.

Many times the ENG record modifies the subjective clinical observation. For example, during the ENG test of case 15, the examiner who watched the eyes gained the impression of a reduced caloric response with grossly irregular eye movements. The subsequent analyisis of the ENG chart showed perfectly regular and rhythmic nystagmus. However, we see a constant succession of nystagmus beats to the right and left reminiscent of a pendulous nystagmus (Fig. 11).

Distinctly different from these observations of heterodirectional beats and pendulous motions was the following type of nystactic dicrotism. In Figure 12, we see a pair of isodirectional nystactic beats of both eyes at the rate of one per second. At first, that is at the left of the curve, there appears a pair of beats separated by a time interval of 0.2 sec. After a pause of about 0.6 sec, a second pair of isodirectional beats is seen. This is followed after 0.8 sec by a couple of beats which are 0.4 sec apart. The remaining right half of the graph shows three further pairs of isodirectional beats with time intervals of about 0.2 sec and separated by pauses of 0.6 to 0.8 sec.

CONCLUSIONS

After many years of specialized interest, and 20 years since the discovery of the electrophysiologic basis of nystactic recording, the method of electronystagmography is now ready to emerge from the realm of theoretical investigation into the domain of practical application. It remains to arrive at a precise calibration and a standardized procedure, in order to present the clinician with a reliable and simple tool of routine examination. A perusal of the literature seems to indicate that the time has come to proceed with such attempts at calibration and uniform registration. One may compare the present position of nystagmography with the situation of audiometry 30 years ago. It will probably require considerably less effort to promote ENG to a level comparable with the present advance of audiometry.

This comparison of the precise measurements of hearing and of balance appears justified from another viewpoint. Audiometry has superseded the classical methods of tuning fork tests, because a more objective, precise and graphic system for the measurement of hearing was needed. Nystagmography bears the same relationship to the subjective methods of visual observations for vestibular nystagmus as does audiometry to tuning fork tests. Therefore, nystagmography is generally accepted as much more precise and informative. It even offers further advantages: compared with pure tone audiometry, the ENG is as accurate but more objective; in comparsion with PGSR audiometry, the ENG appears as objective but more accurate and reliable.

SUMMARY

1. Reviewing the bibliography, one finds a great number of methods and principles for objective nystagmography. The majority of authors seem to prefer the standard equipment for EEG recording, which is readily available in large hospitals. Various modifications of procedure indicate the need for a preferable and uniform system of ENG.

2. At the present stage, it seems most important to arrive at a precise calibration and standardized procedure. Once these will be achieved, ENG will become as widely accepted as audiometry is now.

3. We defined the most important details of our present ENG techniques and described a number of general observations which are the basis for further investigations. In particular, we reported three peculiar patterns of caloric nystagmus which were observed several times, namely, a bipolarity of nystagmus, a form of pendulous nystagmus, and dicrotic nystagmus.

218 Second Ave.

REFERENCES

1. Aschan, G., and Bergstedt, M.: Non-vestibular Nystagmus; A Nystagmographic Investigation. Acta Soc. Med. Upsalien 16:1-2:1-13, 1955.

2. Aschan, G., Bergstedt, M., and Stahle, J.: Nystagmography. Recording of Nystagmus in Clinical Neuro-otologic Examinations. Acta Otolaryng. (Stockholm) 46:Suppl.129, 1956.

3. Aso, J.: Analytic Observation on the Labyrinthine Nystagmus by Electronystagmography. The Relation of the Rotation of the Nystagmus with the Vision. Acta Med. Biol. (Niigata) 1:4:295-304, 1954.

4. Bergman, P., Nathanson, M., and Bender, M.: Electrical Recordings of Normal and Abnormal Eye Movements Modified by Drugs. Archives Neurol. and Psychiatr. 67:357 (Mar.) 1952.

5. DeKleyn, A., and Storm Van Leuwen, W.: Ueber vestibulaere Augenreflexe. Graefes Archiv. Ophthalm. 94:316, 1917.

6. Dewar, J.: The Physiological Action of Light. Nature 15:433, 1877.

7. Dieterle, P., and Monnier, M.: Electronystagmography in Man; Principle and Technique. Pract. Oto-Rhino-Laryng. (Basel) 17:3:164-172, 1955.

8. Glorig, A., and Mauro, A.: Clinical Electronystagmography. ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY 59:146, 1950.

9. Henriksson, N. G.: An Electrical Method for Registration and Analysis of the Movements of the Eyes in Nystagmus. Acta Oto-Laryng. (Stockh.) 45:1:25-41, 1955.

10. Henriksson, N. G.: The Correlation Between the Speed of the Eye in the Slow Phase of Nystagmus and the Vestibular Stimulus. Acta Oto-Laryng. (Stockh.) 45:2:120-136, 1955.

11. Hoffman, A. C., Wellman, B., and Carmichael, L.: A Quantitative Comparison of the Electrical and Photographic Techniques of Eye Movement Recording. J. Exper. Psychol. 24:40, 1939.

12. Jung, R.: The Registration of the Post-Rotatory and Optokinetic Nystagmus and the Optic Vestibular Integration in Man. Acta Oto-Laryng. (Stockh.) 36:3-4:199-202, 1948.

13. Jung, R., und Mittermaier, R.: Zur objektiven Registrierung und Analyse verschiedener Nystagmusformen. Archiv. Ohren-usw. 146:410, 1939.

14. Kirsten, R., und Schoepfer, H.: Disturbances of Electronystagmography Due to Closing of the Eyelids. Archiv. Ohren-usw. Heilk. 168:3:215-219, 1955.

15. Kristensen, H. K., and Zilsstorff-Pedersen, K.: Optical Nystagmography in the Differential Caloric Test ad modum Fitzgerald-Cawthorne-Hallpike. Acta Oto-Laryng. 43:Suppl.109:82-93, 1953.

16. Kuilman, J.: Nystagmography during Counter-rolling of the Eyes in Man. A.M.A. Archives Otolaryngol. 67:424, 1958.

17. LeHeux, J., and DeKleyn, A.: Proc. Royal Acad. Amsterdam 38:470, 1935.

18. Linthicum, F. H.: Nystagmography. A Method for the Graphic Recording of Nystagmus During and After Turning and of Caloric Nystagmus. Archives Otolaryng. 32:464, 1940.

19. Mahoney, J. L., Harlan, W. L., and Bickford, R. G.: Visual and Other Factors Influencing Caloric Nystagmus in Normal Subjects. A.M.A. Archives Otolaryng. 66:46, 1957.

20. Marg, E.: Development of Electro-oculography. Archives Ophthalmol. 45: 169, 1951.

21. Meyers, I. L.: Electronystagmography. Archives Neurol. and Psychiat. 21: 901, 1929.

22. Mittermayer, R.: Results of Nystagmographic Studies. Pract. Oto-Rhino-Laryngol. 17:179, 1955.

23. Monnier, M., and Hufschmidt, H.: Electrooculography and Electronystagmography in the Human. Helv. Physiol. Pharmacol. Acta 8:2:C30-C32, 1950.

24. Montandon, A.: A New Technique for Vestibular Investigation. Acta Otolaryngol. (Stockholm) 44:5-6:594-596, 1954.

25. Montandon, A.: Analysis of the Rototary Nystagmus by Electronystagmography. Acta Otorhinolaryng. Belg. 9:3:328-331, 1955.

26. Montandon, A., and Monnier, M.: Analysis of the Vestibular Nystagmus by Electronystagmographic Methods. Annales d' Oto-laryng. (Paris) 68:11,12:761-765, 1951.

27. Montandon, A., and Monnier, M.: A New Technique for Vestibular Investigation. Acta Otolaryng. (Stockh.) 44:5-6:594-596, 1954.

28. Montandon, A., Monnier, M., and Russbach, A.: A New Technique of Vestibular Rotatory Stimulation and of Electrical Recording of Nystagmus in Man. Annals of Otology, Rhinology and Laryngology 64:3:701-717, 1955.

29. Montandon, A., and Russbach, A.: Les Données de l'Eléctronystagmographie dans l'Examen Vestibulaire. Revue d'Otoneuroophthalm. (Paris) 27(6):382, 1955.

30. Mowrer, O. H., Ruch, T. C., and Miller, N. E.: Corneo-retinal Potential Difference as the Basis of the Galvanometric Method of Recording Eye Movements. Amer. J. Physiol. 114:423, 1936.

31. Ohm, J.: Untersuchungen des Augenzitterns. Alexander-Marburg-Brunner: Handb. Neurol. d. Ohres. 1:1089; Berlin-Wien: Urban und Schwarzenberg, 1921.

32. Perlman, H. B., and Case, T. J.: Nystagmus: Some Observations Based on an Electrical Method for Recording Eye Movements. Laryngoscope 49:217, 1939.

33. Pfaltz, C. R., and Richter, R.: Photolectric Registration of Nystagmus. Pract. Otolaryng. (Basel) 18:263-271, 1956.

34. Pivotti, G., and Lucarelli, A.: I Problemi tecnici della registrazione nistagmografica. Minerva Otolaryngol. (Torino) 5:4:191-196, 1955.

35. Pivotti, G., and Lucarelli, A.: Speed of the Slow Component and the Duration in the Caloric Nystagmus. Acta Otolaryng. (Stockh.) 46:Suppl.125:29, 1956.

36. Reich, M. S.: A New Effort to Evaluate Vestibular Function. Revue Otoneuroophthal. 27:1:12-17, 1955.

37. Rossberg, G., and Kessler, G.: Nystagmography of Rototary Nystagmus. Z. Laryng. Rhinol. Otol. 32(7-8):472-477, 1953.

38. Schott: Ueber die Registrierung des Nystagmus und anderer Augenbewegungen vermittels des Saitengalvanometer. Dtsch. Archiv Klin. Med. 140:79, 1922.

39. Stahle, J.: Electronystagmography in the Caloric Test. Acta Soc. Med. Upsalien. 61:5-6:287-332, 1957.

40. Suzuki, T., and Yamamuro, S.: Electronystagmography. Otolaryngology, Nippon Igoku Zasshi K. K. 22:3:14-18, 1950.

41. Torok, N.: Qualitative Evaluation of Vestibular Nystagmus. Eye, Ear etc. Monthly 31:147-150 (Mar.) 1952.

42. Torok, N.: The Technique of the Electrical Recording of Vestibular Nystagmus During Rotation in Man. Revue de Laryngol. (Bordeaux) 74:7-8:413-423, 1953.

43. Torok, N., Guillemin, V., and Barnothy, J. M.: Photoelectric Nystagmography. Annals of Otology, Rhinology and Laryngology 60-4:917-926, 1951.

44. Van Dishoeck, H. A., and Nijhoff, P.: Vestibular Investigations by Means of an Optic Sensation. Acta Otolaryng. (Stockholm) 44:5-6:597-607, 1954.

45. Van Gemert, A. G. M., and Duyff, J. W.: A New Nystagmograph. Acta Physiol. Pharmac. Néerl. 3:299, 1954.

46. Wojatschek, W.: Ueber einige paradoxe Faelle bei der funktionellen Pruefung des Labyrinths. Archiv Ohrenheilk. 77:230, 1908.

XI

ELECTROPHYSIOLOGICAL STUDIES OF THE LABYRINTH OF THE GUINEA PIG

I. THE DC RESTING POTENTIALS OF THE SEMICIRCULAR CANALS

D. Trincker, M.D.

Erlangen, Germany

Since the early times of Mach, Breuer, Crum Brown, and Ewald, the acoustical and the non-acoustical part of the vertebrate labyrinth have been thought to be two separate receptor systems, connected with each other only topographically or by phylogenetic and ontogenetic development, but characterized by a behavior, functionally rather different. At present, however, the analysis of the biopotentials seems to make comparable the processes, in both cases being involved in the transformation of the adequate mechanical stimulus into receptor excitation.

Inside the cochlear partition and in the perilymph of both scalae, von Békésy[1-3] measured the dc resting potentials.[4] This work, very successful indeed, was confirmed by Tasaki, Davis, and Eldredge,[5] and by Gisselsson.[6] Therefore, it seemed a rather interesting task to check the analogous potentials in the nonacoustical part of the ear labyrinth.

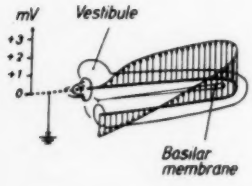
The measuring equipment contained two electrometer valves (Valvo 4060) in a bridge circuit with a high sensitive galvanometer. The one received the potential from the measuring electrode against an indifferent one, the other from a reference electrode likewise against the indifferent electrode. As microelectrodes, glass capillaries were used, filled with silver solder (according to Svaetichin[7]). For measuring outside the membranous labyrinth they were 10 to 25 μ thick at the point, for measuring inside the ampulla even less than 1 μ.

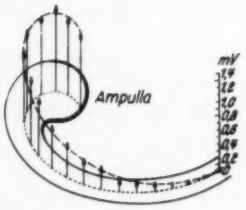
The measurements in the perilymph surrounding the ampulla and the membranous semicircular canal yielded the existence of a posi-

From the Physiological Institute of the University, Erlangen, Germany.

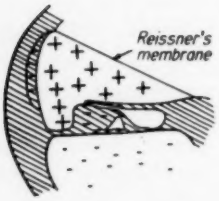
Cochlea (v. Békésy) | Semicircular canals (Trincker)

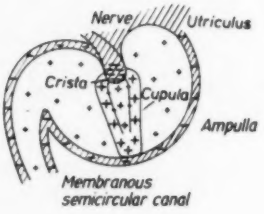
Resting potentials of the perilymphatic space:





Resting potentials of the endolymphatic system:





Resting potentials against the perilymph:

Walls of the endolymphatic system:	about −20mV		−9,0 to −22,0mV
Endolymph:	+50mV		+38,5 to +43,0mV
		Cupula, surface:	+63,0 to +75,5mV
		Cupula, interior:	−6,5 to +75,0mV
Cells of Hensen and Claudius:	−40mV	Cells of the crista ampullaris:	−38,5 to −57,0mV

Fig. 1.—D.C. resting potentials of the labyrinth of the guinea pig.

tive potential against the outer surface of the bony wall. This potential rose from the canal to the middle of the ampulla about 1.0 to 1.5 mV (Fig. 1).

Against the outer side of the crista ampullaris all the other surfaces of ampulla and canal showed positive potentials with a maximum in the middle of the ampulla. Here, the potential amounted to 550 to 635 μV, in the marginal zones of the ampulla and over the adjacent part of the canal to 210 to 240 μV. This potential maximum was abolished after rinsing the cupula out of the ampulla (by an experimentally produced endolymph streaming). A potential reversal was observed during anoxia or after damage of the cupula.

Inside the walls of the ampulla and of the canal, a negative potential amounting to 9.0 to 22.0 mV against the perilymph was found. The endolymph showed rather constant values, 38.5 to 43.0 mV positive against the perilymph (Fig. 1). At the surfaces of the cupula, a higher positive potential was measured: 63:0 to 75.5 mV. The potentials inside the deeper layers of the cupula were rather varying. The positive potential amounted to 65 to 75 mV near the crista and to 55 to 65 mV near the top of the cupula. But between these higher positive potentials, there existed much lower ones which dropped even to weak negative values (–6.5 mV). These potential decreases were rather frequent and deep near the crista, but rare and small near the top of the cupula. The spatial distances from one to the other point of lower potential were of average distance of the hair-like processes, roughly estimated from the number of hair cells in the crista surface.

The crista showed a potential, always negative against the perilymph: 38:5 to 43.5 mV in the lateral parts, something more inwards 42.0 to 57.0 mV. Like the perilymphatic potential, the positive potential of the endolymph, rather high in the ampulla, decreased markedly along the canal. There never existed any significant difference between the potentials from the horizontal canal and its ampulla on the one hand and those from the vertical canals and ampullae on the other.

These results from the nonacoustic part of the labyrinth are generally in accordance with the measurements of von Békésy in the cochlea.

A more detailed communication is published in German in the Pflüger's Archiv f. d. ges. Physiologie 264:351-382, 1957. This work was supported by a grant-in-aid of the Deutsche Forschungsgemeinschaft. The author's special thanks for sug-

gestion and invaluable advice are due to Professor Dr. O. F. Ranke, Director of the Physiological Institute of the University of Erlangen.

REFERENCES

1. Békésy, G. von: DC Potentials and Energy Balance of the Cochlear Partition. J. Acoust. Soc. Am. 23:576, 1951.

2. Békésy, G. von: DC Resting Potentials Inside the Cochlear Partition. J. Acoust. Soc. Am. 24:72, 1952.

3. Békésy, G. von: Gross Localization of the Place of Origin of the Cochlear Microphonics. J. Acoust. Soc. Am. 24:399, 1952.

4. Ranke, O. F.: Physiologie des Gehörs (Lehrbuch d. Physiol. in Einzeldarst.). Berlin, Göttingen, Heidelberg, 1953.

5. Tasaki, I., Davis, H., and Eldredge, D. H.: Exploration of Cochlear Potentials in Guinea Pig with a Micro-electrode. J. Acoust. Soc. Am. 26:765, 1954.

6. Gisselsson, L.: Neuere Probleme des Cochleaeffektes. Arch. Ohr-usw. Heilk. 167:274, 1955-56.

7. Svaetichin, G.: Electrophysiological Investigations on Single Ganglion Cells. Acta Physiol. Scand. 24:Suppl.86, 1951.

II. THE CHANGES OF THE DC POTENTIALS INSIDE THE AMPULLAE OF THE SEMICIRCULAR CANALS DURING EXPERIMENTAL CUPULA DEVIATIONS

D. Trincker, M.D.

In the preceding communication, the author reported his results concerning the dc resting potentials of the semicircular canals. But a mere inventory of existing potential differences would be a rather unsatisfying upshot. A quite more interesting question arose here, the question whether or not changes of the resting potentials occur following adequate stimulation by experimental cupula deflections. Fortunately, he had learned the methods to produce experimental cupula deviations of the late Prof. Dr. Steinhausen.[1-3] But these methods involved an opening of the membranous labyrinth, of the partition wall between endolymph and perilymph. New methods had to be developed to avoid the breakdown of the potential difference between endolymph and perilymph.

The first way to produce endolymph movements was compressing the membranous canal by two counter-directed streams of warm Ringer's solution. The membranous canal was embedded in an artificial gelatine wall, occluding the perilymphatic space. Directing

the streams to one side of the gelatine wall or the other, endolymph movements and the following cupula deviations were produced in both directions. The second way was ligating the membranous canal and compressing it on both sides of the ligature by gradually pulling on circularly applied thin human hairs. The third way was embedding the canal in gelatine and carefully introducing a very fine capillary to exercise both pressure and suction forces.

The optical properties of the living cupula do not permit an immediate visual discrimination against the endolymph. Therefore, in order to get an exact control of the degree of cupula deflection it must be stained. China-ink, diluted with Ringer's solution, was instilled by a microcapillary.

At first, measuring at the surface of the ampulla, a shift of the potential maximum during cupula deviations was detected. In the case of deviations of extreme degree, this shift of the maximum corresponded obviously with the actual cupula displacement. But this phenomenon seemed not to be of any physiological significance. However, together with the maximum shift substantial potential changes occurred, though they were rather weak and much more exactly measurable by recording the analogous changes inside the ampulla.

During experimental cupula deviations (of a degree between 25° and 80°, in steps of 5°), the potential changes were measured in the endolymph, at the cupula surface, and in the lateral parts of the crista ampullaris, bearing hair cells. In the crista of the horizontal (i.e., lateral) ampulla, an utriculopetal cupula deviation always produced a potential decrease, an utriculofugal one a potential increase. In the anterior vertical ampulla, the potential changes were in all cases of opposite direction. In other words, a depolarization was caused by utriculopetal cupula deflections in the horizontal ampulla and by utriculofugal deflections in the anterior vertical; hyperpolarization was caused by utriculofugal deflections in the horizontal ampulla and by utriculopetal ones in the anterior vertical. (The posterior vertical ampulla, not checked here, must behave like the anterior following Ewald's law.) The potential differences were the highest in the crista, markedly lower at the cupula surface, and the lowest in the endolymph. The accompanying graph (Fig. 1) shows the potential changes in the crista.

There, as an additional phenomenon, a potential difference was observed between the both sides of the crista, never occurring at rest, but rising with increasing degree of cupula deflection. The potential

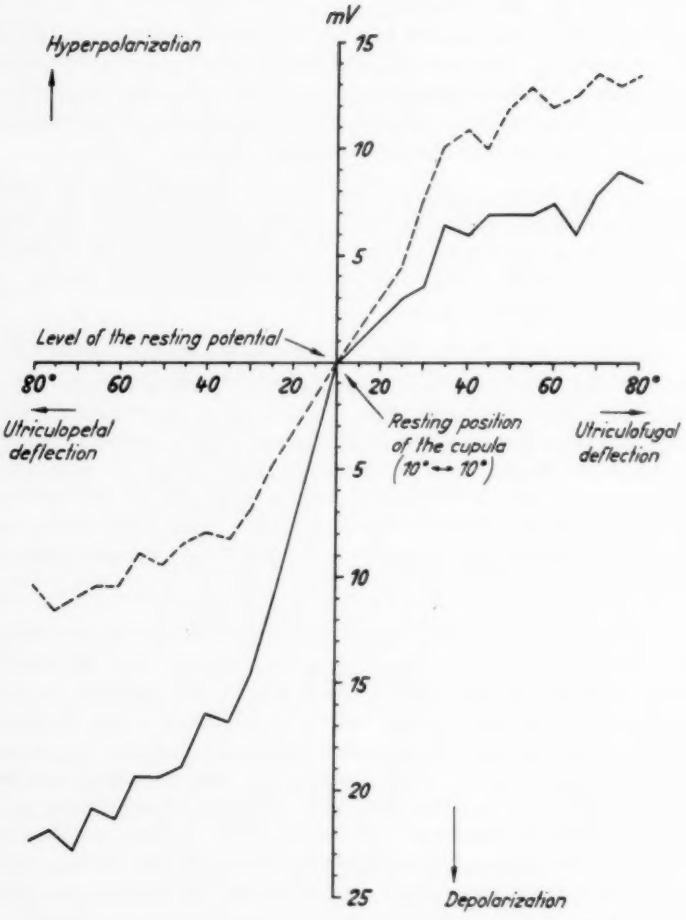


Fig. 1.—The potential changes inside the crista of the horizontal ampulla during experimental cupula deflections, showing the depolarization by utriculopetal deflections and the hyperpolarization by utriculofugal ones, with the appearance of potential differences between both sides of the crista. Full lines: canal-side of the crista; dotted lines: utriculus-side of the crista. Abscissa: Degree of cupula deviation (i.e., the angle between a line connecting the middle of the top of the cupula in resting position with the middle of the crista, and a second line, connecting the leading edge of the top of the deflected cupula with the middle of the crista). The resting position of the cupula corresponds with an angle of 10° in both directions; therefore, the value of 10° is taken for zero. Ordinate: Potential changes in mV. The resting potential is taken for zero.

change was more pronounced at the side opposite to the direction of the deflection, i.e., at the canal-side of the crista in the case of an utriculopetal movement, and at the utriculus-side in the case of an utriculofugal one. This predominating side is identical with the side upon which the hair-like processes of the sensory cells must be more stretched than on the other side, respectively.

The curves of the relation between the value of the potential changes and the degree of cupula deviation were S-shaped (when regarded for both directions, see Fig. 1). The range of physiologically important deviations (usually of very little degree) corresponds with the middle, steep and linear part of the S-curve.

These findings are in very good accordance with the work of O. Lowenstein[4-9] dealing with the action currents from the ampullar nerve. Lowenstein[7,8] has studied the effect of galvanic polarization on its impulse frequency. An ascending current (depolarizing the sensory epithelium of the crista) produced an increase of the frequency; a current descending from the crista (and hyperpolarizing it) made a decrease or even abolition of the resting discharges. Lowenstein postulated from these results the existence of corresponding generator potentials. Using adequate stimulation in both directions, Groen, Lowenstein, and Vendrik[6] obtained an S-shaped curve, too, for the frequency changes of the nerve impulses.

The depolarization and hyperpolarization responses of the ampullar hair cells seem to indicate rather obviously an analogy to the behavior of the cochlear hair cell potentials, described by Tasaki, Davis, and Eldredge.[10] The authors recorded the changes in the positive potential of the endolymph when increasing pressure was applied to scala vestibuli or tympani. Increase of hydrostatic pressure in the scala vestibuli increased the positivity of the endolymph, and increase of pressure in scala tympani decreased it. Such a potential decrease was much greater than the greatest increase ever observed. The latter phenomenon also agrees well with the behavior of the ampullar potentials, shown in Figure 2.

The dc resting potentials are certainly maintained by the metabolism of the sensory cells.[11,12] The bending of the hair-like processes of the cells, caused by cupula deviations, alters the resting metabolism. Such an alteration, excitation or inhibition produces a permeability change of the cell membranes, measurable as a depolarization or hyperpolarization, respectively. These potential changes must represent a connecting link between the mechanical stimulus and the

changes of the nerve impulse frequency.[13,14] The analogous finding in the cochlea is the "dc fall" following adequate, acoustical stimulation, recorded by von Békésy.[11]

REFERENCES

1. Steinhausen, W.: Über den Nachweis der Bewegung der Cupula in der intakten Bogengangsampulle des Labyrinthes bei der Natürlichen rotatorischen und calorischen Reizung. Pflüger's Arch. Physiol. 228:322, 1931.

2. Steinhausen, W.: Über die Beobachtung der Cupula in den Bogengangsampullen des Labyrinthes des lebenden Hechts. Pflüger's Arch. Physiol. 232:500, 1933.

3. Steinhausen, W.: Das Bogengangssystem des inneren Ohres als Wahrnehmungsorgan für Drehungen. Hochschulfilm C 323, 1939.

4. Lowenstein, O., and Sand, A.: The Mechanism of the Semicircular Canal. A Study of the Responses of Single-fiber Preparations to Angular Accelerations and to Rotation at Constant Speed. Proc. Roy. Soc. B 129:256, 1940.

5. Lowenstein, O., and Sand, A.: The Individual and Integrated Activity of the Semicircular Canals of the Elasmobranch Labyrinth. J. Physiol. 99:89, 1940.

6. Groen, J. J., Lowenstein, O., and Vendrik, A. J. H.: The Mechanical Analysis of the Responses from the End-Organ of the Horizontal Semicircular Canal in the Isolated Elasmobranch Labyrinth. J. Physiol. 117:392, 1952.

7. Lowenstein, O.: Effect of Galvanic Polarization on the Impulse Discharges from the Horizontal Ampulla of the Isolated Elasmobranch Labyrinth. Nature 172:549, 1953.

8. Lowenstein, O.: The Effect of Galvanic Polarization on the Impulse Discharge from Sense Endings in the Isolated Labyrinth of the Thornback Ray (Raja clavata). J. Physiol. 127:104, 1955.

9. Lowenstein, O.: Peripheral Mechanisms of Equilibrium. Brit. Med. Bull. 12:114, 1956.

10. Tasaki, I., Davis, H., and Eldredge, D. H.: Exploration of Cochlear Potentials in Guinea Pig with a Micro-electrode. J. Acoust. Soc. Am. 26:765, 1954.

11. Békésy, G. von: DC Potentials and Energy Balance of the Cochlear Partition. J. Acoust. Soc. Am. 23:576, 1951.

12. Ranke, O. F.: Bereichseinstellung der Sinnesorgane. Tagg. Biolog. Regelung, Darmstadt, p. 123, 1954.

13. Davis, H., Tasaki, I., and Goldstein, R.: The Peripheral Origin of Activity with Reference to the Ear. Cold Spring Harb. Symp. Quant. Biol. 17:143, 1952.

14. Jielof, R., Spoor, A., and de Vries, Hl.: The Microphonic Activity of the Lateral Line. J. Physiol. 116:137, 1952.

III. THE AC POTENTIALS (MICROPHONICS) FROM THE VESTIBULAR APPARATUS

D. Trincker, M.D.

AND

C. J. Partsch, M.D.

The bending of the hair-like processes is the adequate stimulus for the sensory cells of the vestibular apparatus and of the cochlea, too. Up to the present, however, the opinion has generally been held that the temporal conditions for stimulation would be completely different in both cases.

While the dc receptor potentials upon which one of the present authors reported in the two preceding communications were not as yet been described, ac potentials from the vestibular apparatus had been studied by some previous authors in several animals.

In search of action potentials, Tullio and Storti[1] were probably the first getting microphonics from the semicircular canals of the pigeon. In the same year, Adrian, Craik, and Sturdy[2] studied the labyrinthine ac potentials in the eel, pike, frog, alligator, and Wever and Vernon the tortoise[3,4] (destroying the sacculus abolished the potentials). Zotterman[5] derived microphonics from the sacculus of the pike and burbot (Lota), and Lowenstein and Roberts[6] from the sacculus and utriculus of the ray (Raja). Pumphrey[7] was able to record microphonics from the teleostean utriculus after destruction of the sacculus and the lagena. De Vries and his collaborators[8-10] and Van Eyck[11-15,17] reported in a series of papers their observations concerning the microphonics of the semicircular canals in the pigeon.

Though such a considerable number of lower vertebrates and of sauropsides yielded positive results, Katsuki and Davis[18] could not detect any sign of microphonic activity from the semicircular canals of the kangaroo rat (Dipodomys) after destroying the cochlea. The failure of vestibular microphonics in the sole mammal which was till now tested seemed to be a rather surprising occurrence requiring studies in other species.

The experiments described here were done in guinea pigs whose cochleae were completely destroyed. Unipolar and bipolar recording

actually yielded microphonics from sacculus, utriculus, and all semicircular canals very clearly.

Figure 3 shows records of microphonics (upper curves) due to application of frequencies between 300 and 100,000 cps (lower curves). In this experiment, the alternating pressure was given to the labyrinth by bone conduction.

Applying the tone by air conduction was a rather more difficult task. However, if the vestibule remained intact and perilymph losses were most carefully avoided during the removal of the cochlear turns, this task might be successful. (Such records have been published in the detailed report.)

The first column of Figure 3 shows the microphonics from the scala tympani of the basal cochlear turn, the following columns include the analogous records from the lateral (horizontal) semicircular canal or its ampulla, before and after destroying the cochlea. The stimulus intensity was in all cases 10 db above threshold. If perilymph losses were avoided, there was hardly any difference between the amplitudes of the vestibular microphonics before and after removal of the cochlea.

Except the ultrasonic range, the microphonics were of the order of 80 to 150 μV (maximal values 230 to 290 μV). The threshold of being recognizable was generally something higher for the vestibular microphonics than for the cochlear ones. The lowest threshold values of the vestibular microphonics were found between 2000 and 4000 cps, that is, at somewhat higher frequencies than in the cochlea.

True microphonics were derived from the cochlea up to 100 to 130 kc, from the vestibular apparatus up to 80 to 120 kc, verifiable by the sensitiveness to anoxia or cooling and by the abolition after death. *

Some records, gained by stimulation with lower frequencies of high intensity, yielded synchronized action potentials as well known for the cochlea potentials. The lower the frequency, the easier the

* Keidel and Sick (Z. Biol. 105:443, 1953) recorded microphonics from the cochlea of the cat and guinea pig up to 57.5 kc, Pestalozza and Davis (Amer. J. Physiol. 185:595, 1956) in the latter up to 46 to 50 kc. In experiments with human subjects, Kunze (in: Ultraschall in der Medizin, Hirzel: Zurich, 1949), Kunze and Kietz (Arch. Ohr-etc. Heilk. 155:683, 1949), Pfander (l.c., 1949) and Timm (Z. Laryng. 30:133, 1951) showed the sensation of a very high tone (without pitch discrimination), caused by ultrasonic frequencies up to 175 (or even 200) kc. In the case of a deaf ear, the sensation was lacking.

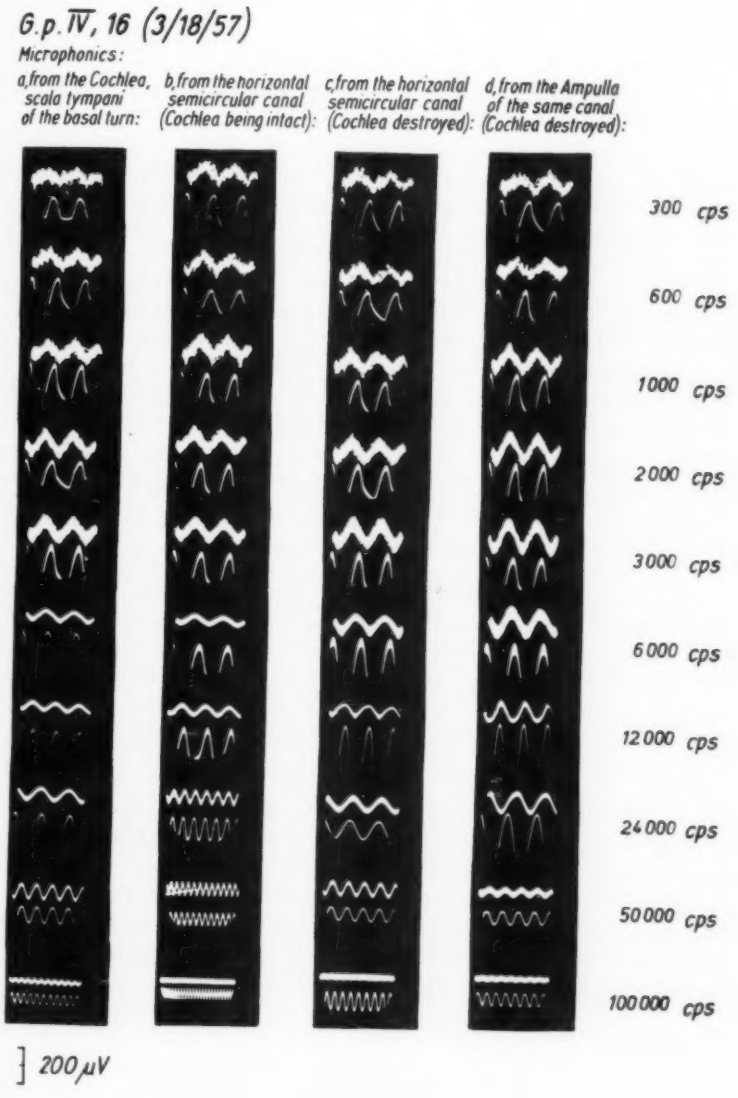


Fig. 3.—Records of microphonics due to application of frequencies between 300 cps and 100,000 cps.

action-potential component could be detected. The upper limit for synchronized action potentials was found between 1600 and 3300 cps in several animals.[19]

In the case of bipolar derivation of microphonics from the canal-side and utriculus-side of the ampulla, the first records showed only a rather small phase-shift; but placing the electrodes, the one at the "roof" of the ampulla (in German, "Ampullendach"), the other below the crista at the wall of the utriculus, delivered nearly opposite phase of microphonics.

After destroying not only the cochlea, but also the sacculus and utriculus, the microphonics were rather markedly reduced (this was doubtless due to the inevitable perilymph and even endolymph losses), but they were clearly still recognizable. Rather striking evidence for the ampulla as a source of microphonics followed from localized cooling. Cold abolished the so-called "first-order-microphonics" (see v. Békésy[20]), but the second-order ones were more cold-resistant.[21] Anoxia exerted almost the same influence upon all hair cells. In the dying animal, the cochlear first-order-microphonics decreased more rapidly than the vestibular ones did.[22]

As a résumé, we may conclude that the hair cells of all labyrinthine organs[23] must electrophysiologically behave in a quite similar manner. All of them can be stimulated by both static displacement and the whole frequency spectrum (coming into question) of mechanical oscillations. Of course, a finer analysis of the alternating pressures may only be performed by the dispersion of the frequencies in the cochlea.[24,25]

A more detailed report is communicated in German at the annual meeting of the Deutsche Physiologische Gesellschaft, Münster 1957, also briefly published in the Pflüger's Archiv f. d. ges. Physiologie 266:77, 1957. This work was supported by a grant-in-aid of the Deutsche Forschungsgemeinshaft. The authors' special thanks for invaluable advice are due to Professor Dr. O. F. Ranke, Director of the Physiological Institute of the University of Erlangen.

PHYSIOLOGICAL INSTITUTE, UNIVERSITY OF ERLANGEN

REFERENCES

1. Tullio, P., and Storti, P.: Boll. Soc. Ital. Biol. Sper. 13:407, 1938.

2. Adrian, E. D., Craik, K. J. W., and Sturdy, R. S.: The Electrical Response of the Auditory Mechanism in Cold-Blooded Vertebrates. Proc. Roy. Soc. B 125: 435, 1958.

3. Wever, E. G., and Vernon, A.: The Sensitivity of the Turtle's Ear as Shown by Its Electrical Potentials. Proc. Nat. Acad. Sci. USA 42:213, 1956.

4. Wever, E. G., and Vernon, A.: Sound Transmission in the Turtle's Ear. Proc. Nat. Acad. Sci. USA 42:292, 1956.

5. Zotterman, Y.: The Microphonic Effect of Teleost Labyrinths and Its Biological Significance. J. Physiol. 102:313, 1943.

6. Lowenstein, O., and Roberts, T. D. M.: The Localization and Analysis of the Responses to Vibration from the Isolated Elasmobranch Labyrinth. A Contribution to the Problem of the Evoluation of Hearing in Vertebrates. J. Physiol. 114:471, 1951.

7. Pumphrey, R. J.: Microphonic Potentials from the Utricle. Nature 143: 898, 1939.

8. de Vries, Hl., and Bleeker, J. D. J. W.: The Microphonic Activity of the Labyrinth of the Pigeon. II. The Response of the Cristae in the Semicircular Canals. Acta Oto-laryng. (Stockh.) 37:298, 1949.

9. Huizinga, E., de Vries, Hl., and Vrolijk, J. M.: Analysis of the Microphonic Activity of the Labyrinth of the Pigeon into the Contributions of the Various Parts. Acta Oto-laryng. (Stockh.) 39:372, 1951.

10. de Vries, Hl., and Vrolijk, J. M.: Phase Relations Between the Microphonic Crista Effect of the Three Semicircular Canals, the Cochlear Microphonics and the Motion of the Stapes. Acta Oto-laryng. (Stockh.) 43:80, 1953.

11. Eyck, M. Van: Potentiels microphoniques dérivés des ampoules des canaux semi-circulaires chez le pigeon. Arch. Internat. Physiol. 57:102, 1949.

12. Eyck, M. Van: Nouvelles recherches sur les potentials dérivés des ampoules des canaux semicirculaires chez le pigeon. Arch. Internat. Physiol. 57:231, 1949.

13. Eyck, M. Van: Potentiels ampullaires et processus d'excitation des canaux semi-circulaires. Arch. Internat. Physiol. 57:434, 1950.

14. Eyck, M. Van: The Effects of Fatigue on the Microphonic Potentials and Action Potentials of the Labyrinths of the Pigeon. Arch. Internat. Physiol. 58:313, 1950.

15. Eyck, M. Van: Potentiels microphoniques dérivés des ampoules des canaux semi-circulaires et lois d'Ewald. Arch. Internat. Physiol. 59:236, 1951.

16. Eyck, M. Van: Acta Otolaryngologica Belgica 3:459, 1949.

17. Eyck, M. Van: Acta Otolog. Belg. 4:233, 1950.

18. Katsuki, Y., and Davis, H.: Electrophysiological Studies of Ear of Kangaroo Rat (Dipodomys). J. Neurophysiol. 17:308, 1954.

19. Stevens, S. S., and Davis, H.: Hearing, Its Psychology and Physiology. New York, 1938 (3rd print. 1948).

20. Békésy, G. von: Gross Localization of the Place of Origin of the Cochlear Microphonic. J. Acoust. Soc. Am. 24:399, 1952.

21. Bornschein, H., and Krejci, F.: Elektrophysiologische Untersuchungen über Temperatureffekte in der Schnecke. Acta Oto-laryng. (Stockh.) 45:467, 1955.

22. Riesco-MacClure, J. S., Davis, H., Gernandt, B. E., and Covell, W. P.: Antemortem Failure of the Aural Microphonic in the Guinea Pig. Proc. Soc. Exper. Biol. and Med. 71:158, 1949.

23. Kuiper, J. W.: The Microphonic Effect of the Lateral Line Organ. Thesis, Groningen (Netherlands) 1956.

24. Békésy, G. von, and Rosenblith, W. A.: The Mechanical Properties of the Ear. In Handbook of Experimental Psychology, edited by S. S. Stevens, New York, 1951.

25. Ranke, O. F.: Physiologie des Gehörs (Lehrbuch d. Physiol. in Einzeldarst.), Berlin, Göttingen, Heidelberg, 1953.

XII

TERATOMA OF THE FLOOR OF THE MOUTH

REPORT OF A CASE

CHARLES R. SMATHERS, M.D.

NEW YORK, N. Y.

Benign teratoma of the neck and floor of the mouth are of interest because of the scarcity of cases presented in the literature. Colp[1] presented an extensive review of dermoid cysts of the floor of the mouth with three case reports and a summary of 32 cases of dermoid cysts from the literature not included in the 1908 collection of Debonnelle. Shore[2] reported on the rarity of sublingual epidermoid (inclusion) cysts having only four cases out of 54,000 surgical specimens at St. Luke's Hospital in New York between 1900 and 1940. Figi[3] reports a case in a 30 year old white male with a large (8 x 6.5 x 4 cm) dermoid cyst of the floor of the mouth above the mylohyoid muscle and in the genioglossi fibers that was delivered intra-orally. He confirms its insidious onset, midline location, infrequent occurrence and congenital origin. Erich[4] comments on the pathologic classification and origin of cysts of the floor of the mouth, where he distinguishes the congenital dermoid cysts (teratoma) from the epidermoid inclusion (sebaceous) cysts. "The teratoma dermoids contain elements derived from any one or all of the three germinal layers, and occur usually in the ovaries and testes." Johnson[5] discusses the differential diagnosis of cysts of the floor of the mouth and includes thyroglossal duct, branchial tumors, dermoids, epidermoid cysts, mucous cyst, polycystoma, traumatic epithelial cysts and ranulas. New[6] also discusses congenital cysts of the floor of the mouth, pharynx and larynx, adding branchial cleft cysts of the pharynx, cystic hygroma and laryngeal cysts to be considered for differential diagnosis.

The diagnosis of a congenital cyst of the floor of the mouth should be considered whenever there is a non-tender mass of insidious onset. The presence of the cyst may or may not be noted from birth.

From the records of the Otolaryngology Department of the Manhattan Eye, Ear and Throat Hospital.

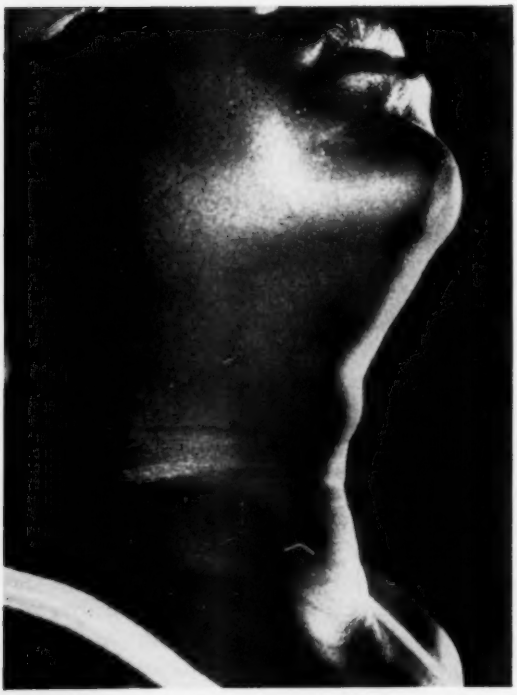


Fig. 1.—Pre-operative appearance of the teratoma at the level of the hyoid bone.

The cyst can displace the tongue to either side or produce an external mass in the neck. Cysts of the floor of the mouth can occur above, in, or below the mylohyoid muscle and may attach to the hyoid bone depending upon their extent and size.

The age group where the cysts of the floor of the mouth most commonly occur is between 15 and 35 years. The sex predilection is equal. The adult age group in which the cysts occur has been explained by the rapid growth during adolescence, however, with increasing suspicion and accurate diagnosis they may be detected in an earlier age group because of their congenital origin. The earliest age at which a teratoma was reported was by Meyer.[7] His patient was a Negro child two days old. An additional case is presented below.

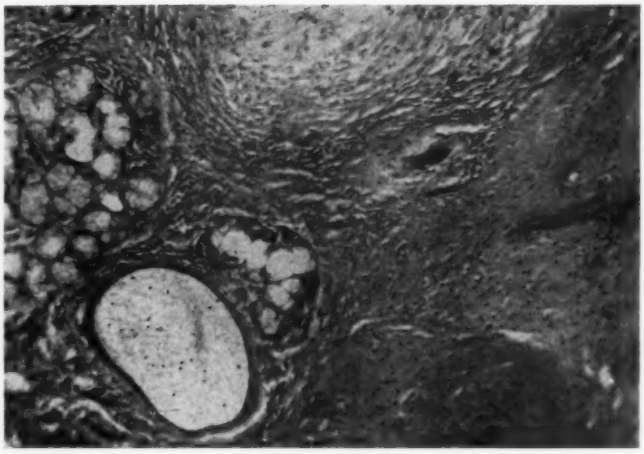


Fig. 2.—Photomicrograph showing a dilated glandular duct, an area of fibro-elastic cartilage and seromucinous glands.

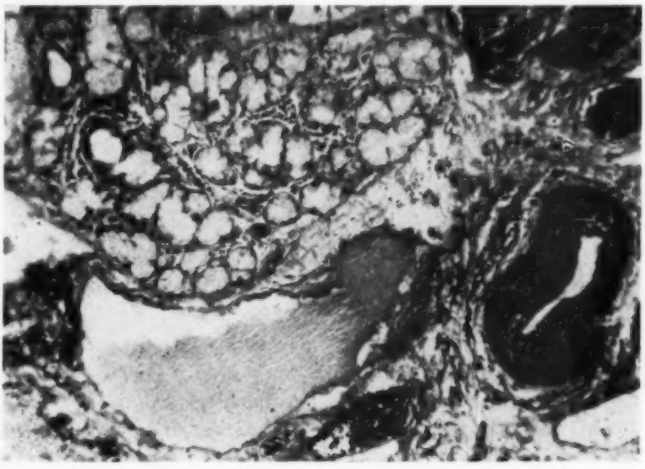


Fig. 3.—Photomicrograph showing a dilated lymphatic with endothelial lining, seromucinous glands, metaplasia of glandular duct epithelium.

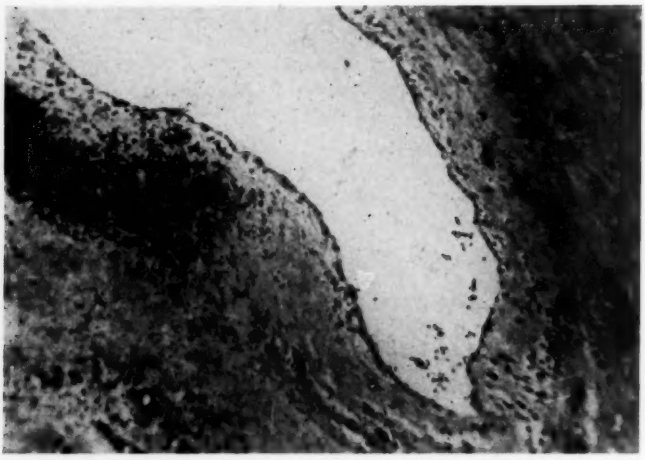


Fig. 4.—Photomicrograph showing detail of endothelial lining of a large dilated lymphatic with thickening of the vessel wall with lymphatic reaction.

REPORT OF A CASE

The patient, F.S., was a four year old colored male who had a lump under his chin, noticed by his parents for the past two years. The mass was non-tender, movable, at the level of the hyoid bone, mid-line, 3 x 4 x 2 cm in size. It was regarded pre-operatively as a thyroglossal cyst. I_{131} scanning revealed less activity over the cyst than laterally over the thyroid lobes. The remainder of the laboratory studies were within normal limits; physical examination was normal. Past medical history and family history were non-contributory.

The patient was operated upon April 15, 1958, under general endotracheal anesthesia. The cyst was approached externally by a transverse incision. The cyst extended to the base of the tongue and enveloped the body of the hyoid bone. The mid-portion of the hyoid bone was removed with the cyst as well as a portion of the base of the tongue, so that when the cyst had been excised the epiglottis was visible through the pharyngostoma. The closure of the pharynx was performed in a transverse manner, a feeding tube inserted through the nostril and a tracheotomy performed. The child made an uneventful recovery and was decanulated and discharged in 11 days. Pathology report by Dr. John Berg and Dr. Andrew E. Eggston was

as follows: The gross specimen consists of two cystic structures, one measured 1.5 x 1.5 x 1 cm and the other specimen measured 4 x 2.5 x 2 cm. Multiple microscopic sections revealed a stratified squamous surface epithelium which shows slight hyperkeratosis. Deeply beneath the epithelium there are numerous seromucous glands and large dilated blood vessels. There were also present nests of squamous epithelium suggesting a sinus tract. Scattered about there were lymph follicles and a few fragments of fibro-elastic cartilage. The main lesion was a large cystic space lined by a thin endothelial layer of cells which resembled a lymphangioma. The cyst wall consisted of dense fibrous collagenous tissue. Diagnosis: Cystic lymphoid teratoma.

COMMENT

The above case is of interest because it occurred in a child of four years. The character of the cyst was like that of a thyroglossal duct cyst. Complete removal is necessary to prevent recurrence. The above tumor was removed by an external approach with an excellent result.

210 East 64th St.

REFERENCES

1. Colp, R.: Dermoid Cysts of the Floor of the Mouth. Surg., Gynec. and Obst. 40:183, 1925.

2. Shore, B. R.: Sublingual Epidermoid Cysts. Ann. Surg. 108:305 (Aug.) 1938.

3. Figi, F. A., and Dix, C. R.: Dermoid Cysts of the Floor of the Mouth; Report of a Case. Proc. Staff Meet., Mayo Clinic 14:289-293, 1939.

4. Erich, J. B.: Sebaceous, Mucous, Dermoid and Epidermoid Cysts. Am. J. of Surg. 50:672, 1940.

5. Johnson, W. H.: Cysts of the Floor of the Mouth. Annals of Otology, Rhinology and Laryngology 51:917-930, 1942.

6. New, G. B.: Congenital Cysts of the Tongue, Floor of the Mouth, the Pharynx and the Larynx. Arch. Otolaryng. 45:145-158, 1947.

7. Meyer, I.: Dermoid Cysts of the Floor of the Mouth. Oral Surg., Medicine and Pathology 8:1149 (Nov.) 1955.

XIII

THE EFFECT OF CUTTING THE LABYRINTHINE ARTERY ON THE OXYGEN TENSION IN THE LABYRINTH

YASUSHI KOIDE, PH.D., M.D.

MAKOTO YOSHIDA, M.D.

AND

MASARU KONNO, M.D.

NIIGATA, JAPAN

Koide,[1] by the theoretical analysis of the functioning metabolic system of the labyrinth, has concluded that oxygen is the limiting factor of the chemical reactions in the labyrinth. In addition, Koide and associates[2,3] have measured the oxygen tension in the labyrinth and ascertained that the oxygen tension is not decreased by oxygen deficiency of a medium degree. Then it was concluded that this observation coincides with the well-known fact that the cochlear potential shows a high resistance to oxygen deficiency.

In the further study on the attitude of the labyrinth to oxygen a new experimental condition must be devised so that the relation between the cochlear potential and the oxygen tension in the labyrinth may be obtained. The labyrinth is, thermodynamically, an open system and receives the influence of general changes. This makes the interpretation of experimental results more difficulty and complicated. Therefore, if it were converted into a closed system by cutting the labyrinthine artery, a clear-cut experiment would be expected and the change of oxygen tension in the labyrinth would be followed up quantitatively. Maruyama[4] has observed that the cochlear potential declines exponentially as time elapses after cutting the labyrinthine artery.

The present study was undertaken to investigate the change of oxygen tension in the labyrinth after the labyrinthine artery had

From the Department of Otolaryngology, Niigata University School of Medicine, Niigata, Japan.

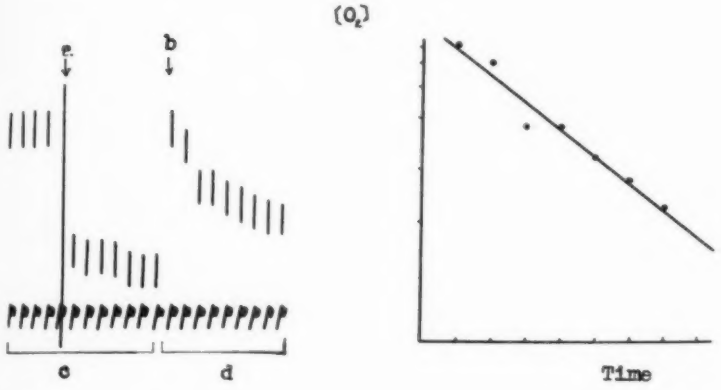


Fig. 1.—The change of oxygen tension in the labyrinth after the labyrinthine artery was cut. The left figure shows oxigraphic recording of oxygen tension. The right figure shows change of oxygen tension in the perilymph plotted on semilogarithmic paper. The oxygen tension was plotted on the logarithmic axis (ordinate), and the time was plotted on the linear axis (abscissa). A straight line was obtained. At (a) cutting. At (b) pt-electrode was withdrawn. (c): Oxygen tension in the basal turn of membranous cochlea. (d): Oxygen tension in the perilymph. Time trace: ten seconds.

been severed and to decide whether or not the labyrinth would be converted to a perfect closed system by this procedure.

RESULTS

A. *The Change of Oxygen Tension after Cutting the Labyrinthine Artery.* By the method of Koide and others,[2] a platinum electrode was inserted into the basal turn of the cochlea of the rabbit and, after cutting the labyrinthine artery, the change of oxygen tension was recorded with oxygraph in the membranous cochlea and the perilymphatic space.

The cutting of the artery was performed in the following way: after the occipital trepanation, an incision of the dura mater was made in the posterior cranial cavity and the cerebellum was widely exposed. Then the cerebellum was displaced with a spatula so that the internal auditory meatus was visible, and the labyrinthine artery was cut with a small scalpel.

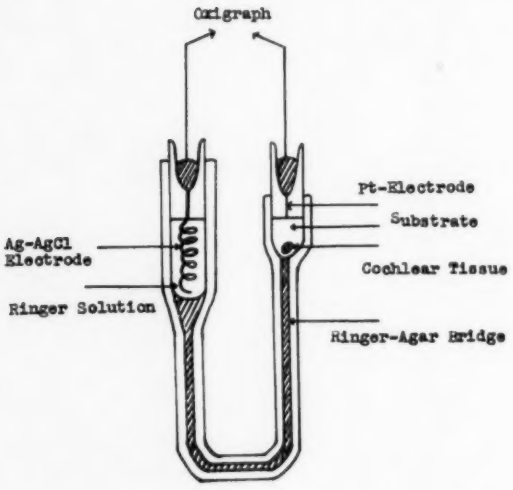


Fig. 2.—Reaction vessel.

After cutting the artery, as shown in Figure 1, the oxygen tension in the membranous cochlea decreased instantly. When the platinum electrode was withdrawn approximately 0.1 mm and the tip was moved from the membranous cochlea to the perilymph, the oxygen tension in the latter decreased rapidly. By plotting this on a semilogarithmic section paper, its exponential course was ascertained.

To analyze a biological phenomenon, the introduction of a thermodynamical concept, entropy production, is quite useful. After the labyrinth has been converted from an open system to a closed system by cutting the labyrinthine artery, the origin of the entropy production in the labyrinth is only the chemical reaction which takes place in it. Because the limiting factor of the chemical reaction in the labyrinth is oxygen, the entropy production in the labyrinth must parallel the change of oxygen tension in it after the labyrinthine artery has been cut. If there were a close relationship between the cochlar potential and oxygen after cutting the labyrinthine artery, the time courses of both should be similar. In fact, this was ascertained in the present study.

Now one question remains. A further investigation is required to decide whether the labyrinth is really converted into a closed system by cutting the labyrinthine artery.

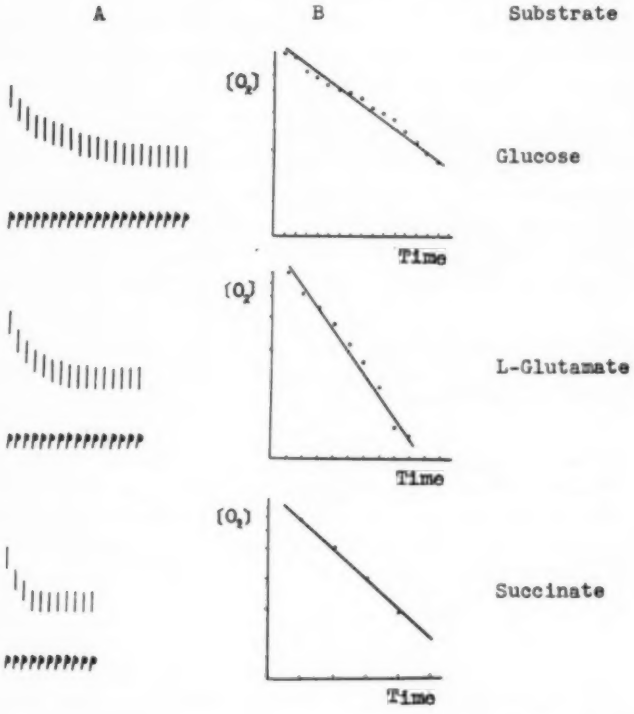


Fig. 3.—Oxygen consumption of the cochlear tissues in the closed system. Section A shows oxigraphic recording of oxygen tension in the closed vessel. Section B shows change of oxygen tension plotted on the logarithmic axis (ordinate), and the time plotted on the linear axis (abscissa). In each experiment a straight line was obtained. Time trace: 30 seconds.

B. *The Change of Oxygen Tension in the Medium Containing the Isolated Labyrinthine Tissues.* To solve this question, whether or not the labyrinth was converted into a closed system by cutting the labyrinthine artery, the isolated labyrinthine tissues were placed in a closed vessel which was apparently a perfect closed system and the decrease in oxygen tension in the medium was followed up, to compare with the results obtained in the previous experiment.

The reaction vessel which was made up specially for this purpose is shown in Figure 2. The medium was made by adding a substrate

to the phosphate-Ringer-solution, the pH of which was 7.2 at a concentration of 15 mM/1. The substrates added were glucose, glutamate and succinate. The reaction vessel was left in a thermostat, the temperature in which was kept at 37° C, and the change of oxygen tension was recorded with oxygraph.

The membranous cochlea of the guinea pig was used as the specimen in this experiment. The animal was killed by cutting the common carotid artery. The labyrinth was isolated in the phosphate-Ringer-solution which had previously cooled below 5° C and only the cochlear tissues were taken out. The elapsed time from death to the completion of the preparation was approximately 20 minutes.

The result is shown in Figure 3. The decrease in oxygen tension in the medium in the vessel was perfectly exponential and the time course was plotted almost linearly on a semilogarithmic paper.

In a closed system the decrease in oxygen tension of the medium was exponential and coincided with the change of oxygen tension after cutting the labyrinthine artery. Thus it may be concluded that the labyrinth was converted from an open system to a closed system by cutting the labyrinthine artery.

CONCLUSIONS

The experimental condition was simplified by cutting the labyrinthine artery and the labyrinth was converted into a closed system. This procedure made possible the quantitative following up of the change of oxygen tension in the labyrinth. The following conclusion was obtained after consideration.

By cutting the labyrinthine artery, the labyrinth was changed into an almost perfect closed system, after the blood flow in the membranous cochlea decreased exponentially. Though the simultaneous recording of the cochlear potential and the oxygen tension in the labyrinth is not possible at the present time and no decisive conclusion can be reached, taking into consideration that Maruyama's experiment, which showed an exponential decrease of the cochlear potential after cutting the labyrinthine artery, a quite close correlation can be assumed between the oxygen tension in the labyrinth and the cochlear potential.

NIIGATA UNIVERSITY SCHOOL OF MEDICINE

REFERENCES

1. Koide, Y.: Introductory Studies on the Chemical-Physiology of the Labyrinth. Zibi Rinsho (Japan) 50:377, 1957, and Acta Med. et Biol. 6:1, 1958.

2. Koide, Y., Konno, M., Kaneko, T., and Yoshida, M.: Changes of the Oxygen Tension in the Labyrinth. Jap. Jour. Otol., Tokyo 61:Suppl.:192, 1958.

3. Koide, Y., Konno, M., and Morimoto, M.: Oxigraphic Measurement of the Oxygen Tension in the Labyrinth. ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY, 1958.

4. Maruyama, N.: Experimental Observations on the Labyrinthine Blood Flow and the Hearing. Jap. Jour. Otol., Tokyo 59:717, 1956.

XIV

RUBELLA IN PREGNANCY

FETAL PATHOLOGY IN THE INTERNAL EAR

J. E. GRAY

NEWCASTLE-UPON-TYNE, ENG.

There have been many clinical accounts of congenital abnormalities following rubella in early pregnancy since the original reports by Gregg[1] in 1941 and Swan et al[2] in 1943. The fetal pathology has been described in a small number of cases only. This report gives the histology of the internal ears of a 53 mm fetus.

CLINICAL DETAILS

The mother developed a severe clinical attack of rubella on the 37th day of pregnancy, i.e., 51 days after the last menstrual period. She had suffered spontaneous abortion after an attack of measles (morbilla) in a previous pregnancy and had one normal child. Abdominal hysterotomy was performed 12 weeks after the last menstrual period because of the mother's mental state. The fetus was 53 mm C.R. length, the clinical dating was thus confirmed.

MATERIAL AND METHODS

The fetus was of normal external appearance. The head, with neck, and the limbs were separated from the trunk and all were fixed in Bouins fluid about one hour after the hysterotomy. The head was several weeks later embedded in paraffin wax and serial sections were cut in the frontal plane at 10 μ.

RESULTS

There were questionable abnormalities in the lens of both eyes, the dental lamina and tooth germs showed abnormalities, the olfactory bulbs were of unequal length, the heart and other viscera of the trunk, the brain and cranial nerves were normal. There was a distinct abnormality of the cochlear duct of both ears. The lesions of the cochlear duct were obvious in the basal coil—less marked in the middle coil and minimal in the apical coil, indeed here they could not be

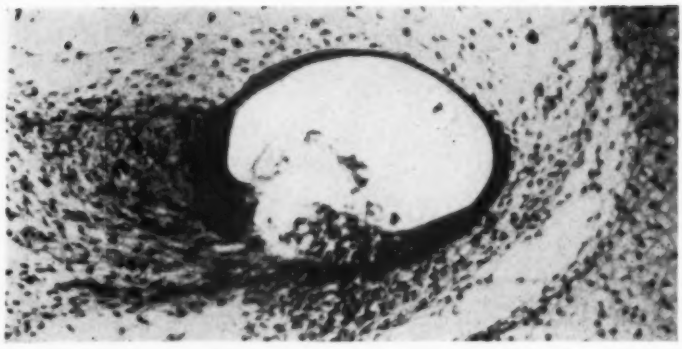


Fig. 1.—Magnification x 200. Basal turn of L. cochlear duct at the level of the f. cochlearis. A large area of cell lysis is present in the basilar membrane.

distinguished from a technical artefact. Both ears showed identical changes. In the basal turn of the cochlea the primordium of Corti's organ displayed an area where the epithelium was absent, an adjacent area, further from the spiral lamina, had spaces between the cells many of which had apparently lost their cytoplasm. Figure 1 shows the basal coil of the cochlea. Figure 2 is the middle coil of the right cochlea. Figure 3 shows the upper part of the basal coil at a higher magnification. The figures to some extent speak for themselves and there can be no doubt that Corti's organ could not have developed normally. The lesion of the basal coil shows what appears to be an infiltration of small round cells. This is probably not the true interpretation, the round cells are more likely to be epithelial nuclei which have lost their cytoplasm. The process of cytoplasmic lysis is seen partially completed in the higher power view in Figure 2.

The utricle, saccule and semicircular canals were normal. The macula of the saccule is shown in Figure 4.

Comparison of these sections with previously reported cases is instructive. Tondury[3] in 1952 showed a photograph of the cochlear duct illustrating a similar but less marked process. Other authors, Nager,[4] Carruthers,[5] and Carruthers et al[6] described much older fetuses or children and their findings are probably end results. The authors quoted above also found that the stria vascularis was smaller than normal and the tendency has been to put down the changes in

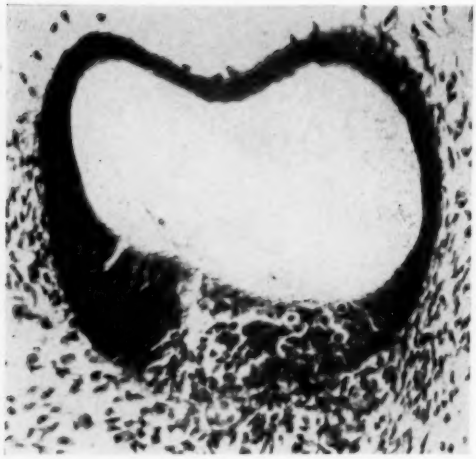


Fig. 2.—Magnification x 320. Upper part of the middle coil of the duct a few sections anterior to the f. vestibuli. The spiral artery can be seen adjacent to the basilar membrane.

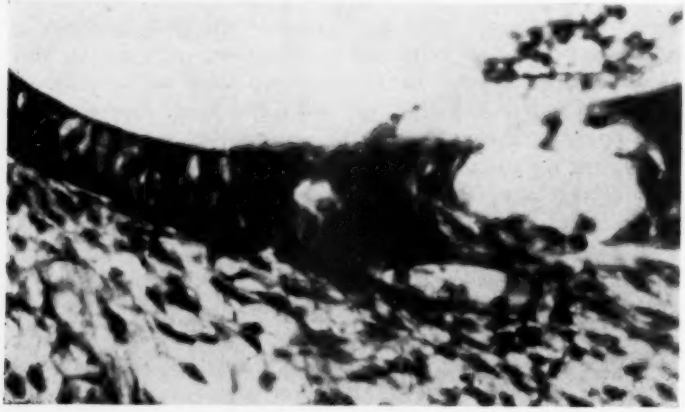


Fig. 3.—Magnification x 580. Basilar membrane of the R. cochlear L. cochlear duct. There is marked cytoplasmic lysis of the epithelium of the basilar membrane. Cell loss is less than in the basal coil.

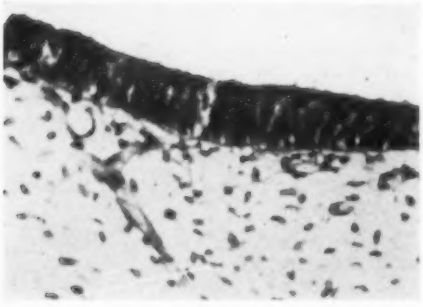


Fig. 4.—Magnification x 320. Macula of L. saccule. Hair-like processes have developed on the neuroepithelial cells. There is no sign of an otolith membrane.

the organ of Corti as secondary to the stria vascularis changes. The lesions described in my case are apparently primary and there seems to be no reason for supposing that they would not have resulted in disorders of Corti's organ like those illustrated by the other authors. It seems that there has been a tendency to incriminate hypothetical primary lesions in blood vessels in order to unify the dispersed sites of damage by the virus (or other toxic agent) in fetal rubella. It would perhaps be more fruitful to admit that at present we do not have an adequate explanation for the sites of election of the disease; it seems unlikely that if the condition were primarily a disease of small blood vessels that the sites of damage would be so restricted. It may be relevant to observe that cell lysis is due to occur in the basilar membrane at a later stage when the spiral sulcus and tunnels are formed.

SUMMARY

The pathology in the internal ear of a 53 mm fetus is described. The mother developed rubella on the 37th day of pregnancy (51 days after L.M.P.). The lesion was apparently lysis of the epithelium of Corti's organ.

The author thanks his colleagues in the University of Durham for their help in examining this problem; in particular, he thanks Professor J. Short and Professor H. Harvey Evers.

REFERENCES

1. Gregg, N. M.: Congenital Cataract Following German Measles in the Mother. Tr. Ophth. Soc. Australia 3:35, 1941.

2. Swan, C., Tostevin, A. L., Moore, B., Mayo, H., and Black, G. H. B.: Congenital Defects in Infants Following Infectious Diseases During Pregnancy. Med. J. Aust. 2:209, 1943.

3. Tondury, G.: Zur Wirkung des Erregers der Rubeolen auf dem menschlichen Keimling. Helv. Ped. Acta 7:103-135, 1952.

4. Nager, R.: Histologic Ear Examinations of Children Following Maternal Rubella. Pract. Oto-rhino-laryng. 14:337-359, 1952.

5. Carruthers, D. G.: Congenital Deaf Mutism as Sequela of Rubella-like Maternal Infection During Pregnancy. M. J. Australia 1:315-320, 1945.

6. Lindsay, J. R., Carruthers, D. G., Hemenway, W. G., and Harrison, M. S.: Inner Ear Pathology Following Maternal Rubella. ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY 62:1201-1218, 1953.

XV

SECRETORY SIALOGRAPHY IN DISEASES EXTERNAL TO THE MAJOR SALIVARY GLANDS

IRVING M. BLATT, M.D.
JOHN E. MAGIELSKI, M.D.
JAMES H. MAXWELL, M.D.
AND
JOHN F. HOLT, M.D.
ANN ARBOR, MICH.

Secretory sialography[1,2] has been a useful aid in determining whether tumors in the submaxillary and parotid regions are within or adjacent to the major salivary glands. This report is concerned with the results of a sialographic study of 31 patients in whom regional swellings external to the salivary glands were present. In all cases the clinical, roentgenographic and (where possible) the operative and histologic findings have been correlated (Table I).

CRITERIA FOR DIAGNOSIS OF EXTRINSIC LESIONS BY SIALOGRAPHY

Scout Films. Preliminary films occasionally make the diagnosis obvious, precluding the use of sialograms. For example, the characteristic mulberry pattern of calcification in a chain of tuberculous cervical lymph nodes is readily identified (Fig. 1A). A destructive, osteolytic lesion of the mandible is also easily discernible (Fig. 1B).

Filling Phase. Complete filling is most essential before any gross deviation from the normal duct pattern is to be accounted for. This is best accomplished by injection of the contrast material through a polyethylene catheter utilizing a closed system of injection.[1] The filling phase shows normal arborization of the duct system with or without displacement (Fig. 2). The common finding is displacement,

From the Departments of Otolaryngology and Radiology, University of Michigan Medical School, Ann Arbor.

TABLE I

THIRTY-ONE PATIENTS WITH LESIONS IN THE SUBMAXILLARY AND PAROTID REGIONS ADJACENT TO THE MAJOR SALIVARY GLANDS

NAME AND REG. NO.	SEX	AGE	AREA INVOLVED	DIAGNOSIS	SIALOGRAM	HISTOLOGIC DIAGNOSIS	QUANTITY PANTOPAQUE INJECTED (ml)
1. M.J. 642871	F	37	Submaxillary	Lymphadenopathy, Inflammatory, Nonspecific	X		0.6
2. H.I. 885146	F	32	Submaxillary	Lymphadenopathy, Inflammatory, Nonspecific	X		0.4
3. C.L. 873779	F	5	Submaxillary	Lymphadenopathy, Inflammatory, Nonspecific	X		0.25
4. M.M. 795601	F	47	Submaxillary	Lymphadenopathy, Inflammatory, Nonspecific	X		0.4
5. L.R. 846222	M	25	Parotid	Lymphadenopathy, Inflammatory, Nonspecific	X		0.6
6. R.S. 810811	M	19	Parotid	Hematoma of Buccal Fat Pad	X		1.0
7. M.P. 193807	M	39	Parotid	Masticator Space Abscess	X	X	0.8
8. D.G. 815433	M	30	Parotid	Masseter Hypertrophy	X		0.70 Right 0.65 Left
9. J.A. 812182	F	47	Parotid	Masseter Hypertrophy	X		0.75
10. J.J. 791438	M	17	Parotid	Masseter Hypertrophy	X		1.0
11. D.C. 815230	F	30	Parotid	Masseter Hypertrophy	X		0.65 Right 0.65 Left
12. N.S. 860368	F	46	Parotid	Phlebolith of Cheek	X	X	0.5
13. L.M. 808607	F	13	Parotid	Bone Cyst of Mandible	X	X	0.6
14. R.B. 804123	F	50	Parotid	Synovial Cyst of Temporo-Mandibular Joint	X	X	1.0
15. S.S. 579687	F	26	Parotid	Chondroma of Temporo-Mandibular Joint	X	X	0.6

16.	M.C. 857684	M	9	Parotid	Temporal Lymphangioma	X	X	0.35
17.	J.G. 793638	M	18	Parotid and Submaxillary	Fibroma Durum of Sensory Cervical Plexus	X	X	0.4 Submax. 0.6 Parotid
18.	J.Z. 871421	M	14	Parotid	Malignant Osteoblastoma of the Mandible	X	X	0.45
19.	E.H. 783786	F	52	Parotid	Lympho-Epithelioma of Nasopharynx with Parotid Lymph Node Metastasis	X	X	0.7
20.	A.W. 801803	F	47	Parotid and Submaxillary	Carcinoma of Nasopharynx with Parotid and Submaxillary Lymph Node Metastasis	X	X	0.7 Submax. 0.9 Parotid
21.	E.W. 776518	F	43	Parotid and Submaxillary	Chemodectoma	X	X	0.4 Submax. 0.6 Parotid
22.	E.P. 178321	F	60	Parotid	Chemodectoma	X	X	0.8
23.	A.K. 854941	M	29	Parotid	Malignant Melanoma of Scalp with Metastasis to Parotid Lymph Nodes	X	X	0.8
24.	F.E. 780905	M	50	Parotid and Submaxillary	Carcinoma of Submaxillary Gland (Recurrent) with Parotid Lymph Node Metastasis	X	X	1.5
25.	I.S. 834761	F	53	Submaxillary	Carcinoma, Base of Tongue with Submaxillary Lymph Node Metastasis	X		0.5
26.	O.S. 783461	M	72	Submaxillary	Carcinoma, Base of Tongue with Submaxillary Lymph Node Metastasis	X	X	0.6
27.	P.F. 322860	F	42	Parotid and Submaxillary	Metastatic Fibrosarcoma Adjacent to Salivary Gland (Recurrent)	X	X	0.6 Parotid
28.	D.O. 812075	F	52	Parotid	Poorly Differentiated Carcinoma of Face, Primary Site Not Determined	X	X	0.5
29.	R.S. 790532	M	58	Submaxillary	Carcinoma Involving Submaxillary Lymph Node, Primary Site Not Determined	X	X	0.5
30.	C.L. 205010	M	48	Submaxillary	Hodgkins Granuloma in a Submaxillary Lymph Node	X	X	0.6
31.	V.W. 626241	F	39	Submaxillary	Epithelial Retention Cyst	X	X	0.75

compression or distortion of the duct system by the adjacent extrinsic mass (Fig. 3). The general architectural pattern of the duct system is preserved; each duct is seen in its entirety, although its shape and configuration will vary with the degree of displacement (Fig. 4). The main duct may be pushed out of position but there is no alteration in the fine detail of the most peripheral duct radicals (Fig. 5). There may be an area of localized narrowing due to pressure and stretching by the expanding extrinsic lesion (Fig. 6). Occasionally a circumscribed radiodensity, quite apart from the duct system may appear as an intrinsic salivary gland lesion because of its seemingly intrinsic position in particular radiographic projections. The sialogram, however, demonstrates its precise location (Fig. 7) and identifies it as a probable phlebolith of the cheek. Such a lesion could easily be confused with a parotid calculus on routine roentgenography.

Emptying Phase. Secretory sialography is valuable in identifying lesions extrinsic to the major salivary glands, whether inflammatory or neoplastic, since complete emptying of the ducts and acini occurs immediately following stimulation (Figs. 2-7). A radiopaque medium of low viscosity such as Pantopaque®, is ideal since it is readily washed out of the duct system by the salivary secretion. Utilization of the filling phase alone makes it difficult to distinguish extrinsic swellings from intrinsic salivary gland diseases in which the glandular architecture may also be preserved.

ROENTGENOGRAPHIC-HISTOLOGIC CORRELATION

The significance of the roentgenographic findings of compression, distortion, displacement with complete emptying of the salivary duct system associated with the presence of an extrinsic lesion is supported by histologic evidence presented in Table I. In twelve patients (cases 19 through 30) in whom metastatic neoplasm was suspected, all demonstrated anaplastic growth in tissue adjacent to the particular parotid or submaxillary salivary gland in question. In each case the contiguous neoplasm was either in a lymph node or in the adjacent primary site. This is demonstrated in the following case report:

REPORT OF A CASE

CASE 27: P.F., a 42 year old housewife, was referred to University Hospital for evaluation of a previously excised malignant connective tissue neoplasm in the left submaxillary region six weeks prior to admission. Physical examination revealed a 2 by 2 cm firm fixed mass at the angle of the mandible which seemed adherent to perioste-

um and appeared to invade or be a part of the inferior aspect of the left parotid gland. A sialogram four days prior to operation revealed posterior displacement and compression (Fig. 3) of the most inferior intraglandular ducts. Emptying was complete on lemon stimulation. At operation residual neoplasm was found contiguous with the lower pole of the parotid gland. The histologic sections showed a poorly differentiated neoplasm in adipose tissue adjacent to salivary gland compatible with a fibrosarcoma. The contiguous parotid gland showed no neoplasm.

SUMMARY

Secretory sialography can serve as a diagnostic aid in identifying inflammatory and neoplastic lesions adjacent but extrinsic to the salivary glands.

The filling phase shows displacement, compression or distortion of the duct system by the adjacent extrinsic mass, but the general architecture is preserved.

Evacuation of the contrast material is complete in the emptying phase. This is the differential point between extrinsic and intrinsic salivary gland neoplasms, since the latter usually show retention of contrast material in post-evacuation films.

UNIVERSITY HOSPITAL

REFERENCES

1. Rubin, P., Blatt, I. M., Holt, J. F., and Maxwell, J. H.: Physiological or Secretory Sialography. ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY 64: 667, 1955.

2. Blatt, I. M., Rubin, P., French, A. J., Maxwell, J. H., and Holt, J. F.: Secretory Sialography in Diseases of the Major Salivary Glands. ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY 65:295, 1956.

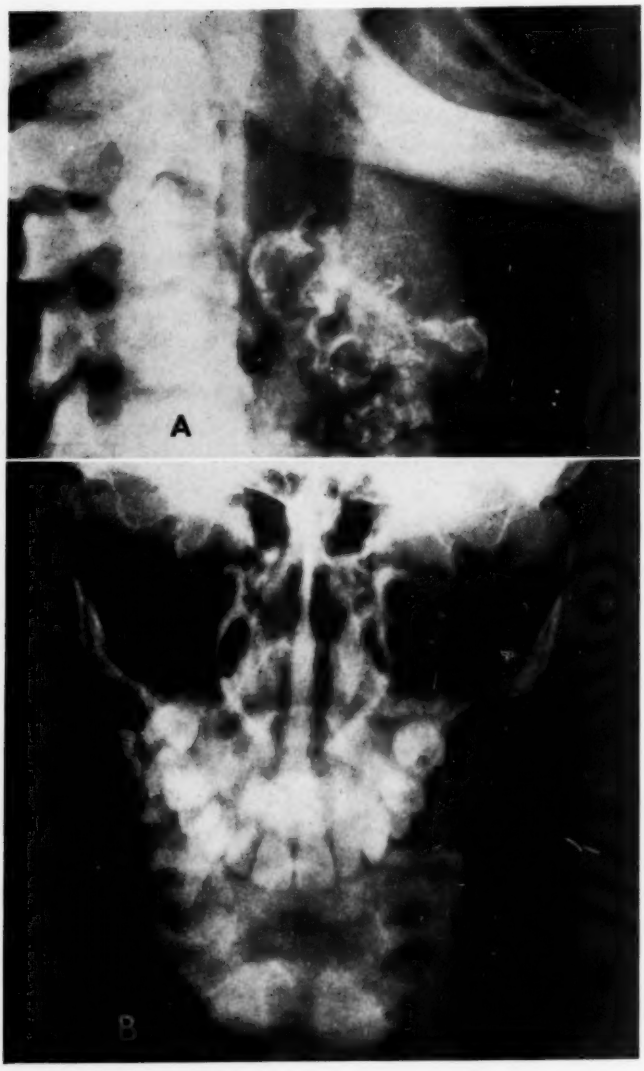


Fig. 1.—(A) Calcified tuberculous lymph nodes in the right submaxillary triangle. (B) Radiograph of a malignant osteoblastoma of the mandible showing osteolytic destruction of bone (arrow). Such lesions adjacent to the major salivary glands preclude the use of sialography.

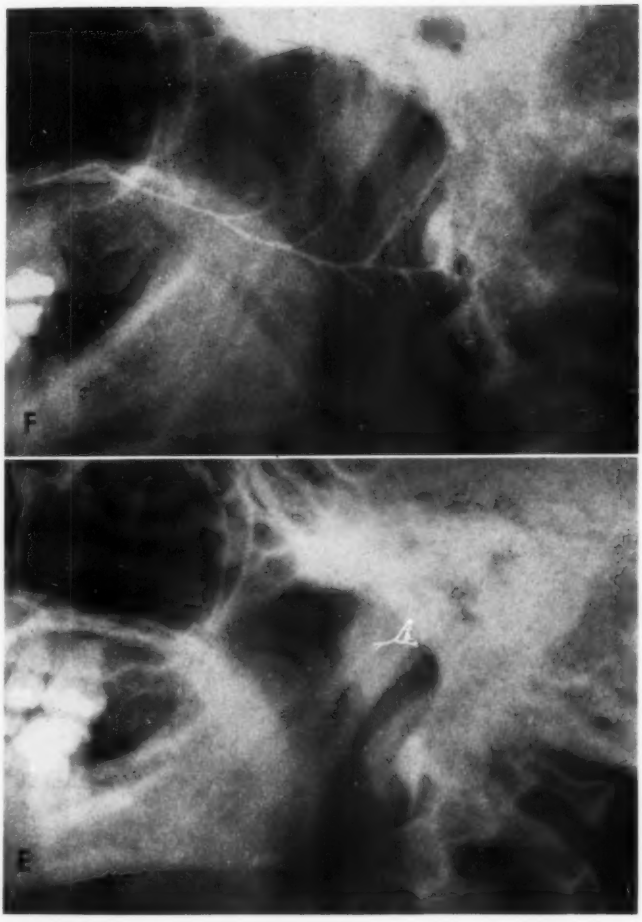


Fig. 2.—Sialogram of case No. 15. The filling phase shows neither displacement, compression nor distortion of the duct system by the adjacent extrinsic mass. Evacuation of the contrast material is complete in the emptying phase. Histologic diagnosis: Chondroma of the temporo-mandibular joint.

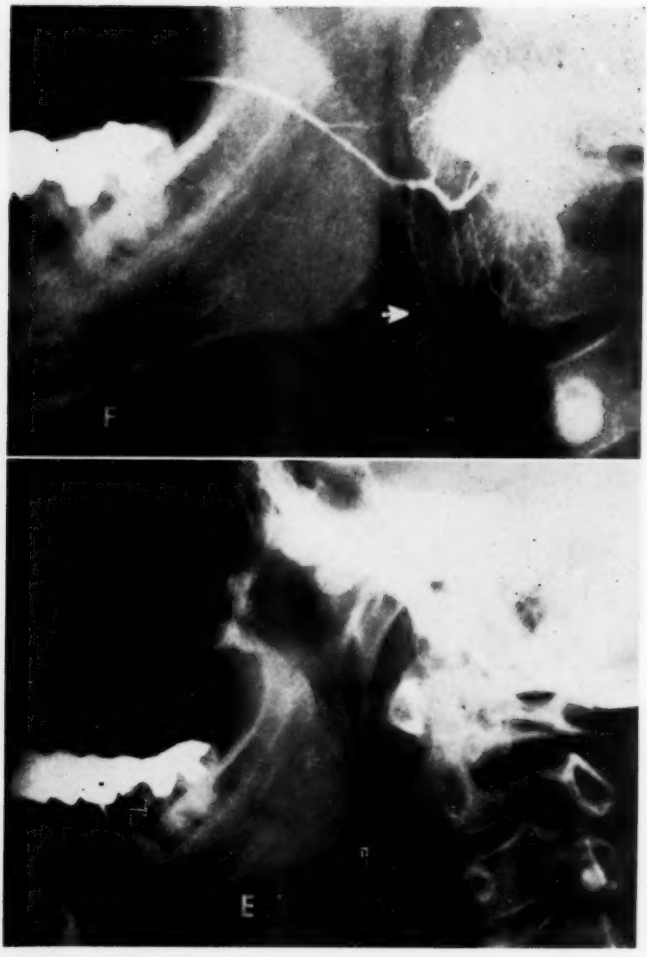


Fig. 3.—Sialogram of case No. 27. The filling phase demonstrates compression and posterior displacement (arrow) of the peripheral duct system in the inferior portion of the superficial lobe of the parotid gland. However, the evacuation of contrast material is complete. Histologic diagnosis: Fibrosarcoma in adjacent adipose tissue.

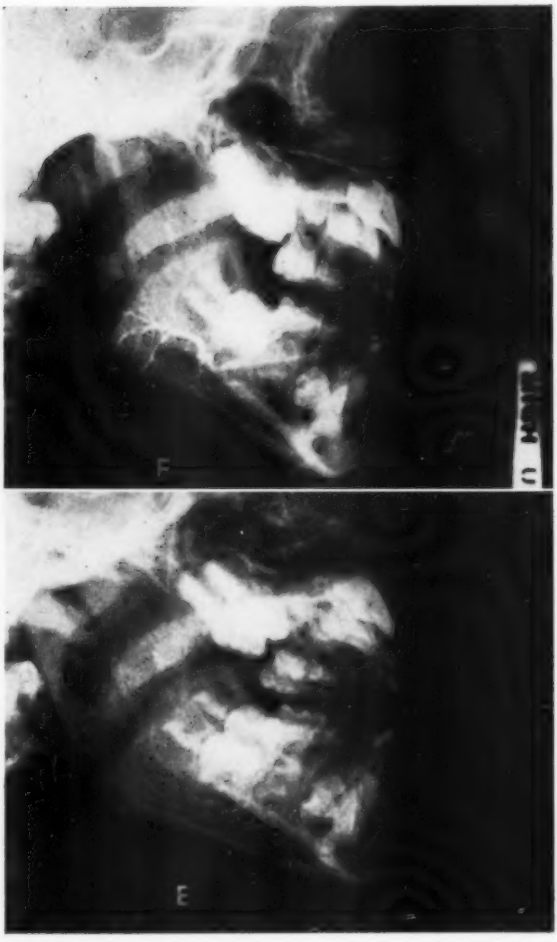


Fig. 4.—Sialogram of case No. 3, a 5 year old girl with submaxillary lymphadenitis. The filling phase demonstrates upward displacement of the left submaxillary salivary gland. The post-evacuation film indicates that the gland has emptied completely and is not involved.

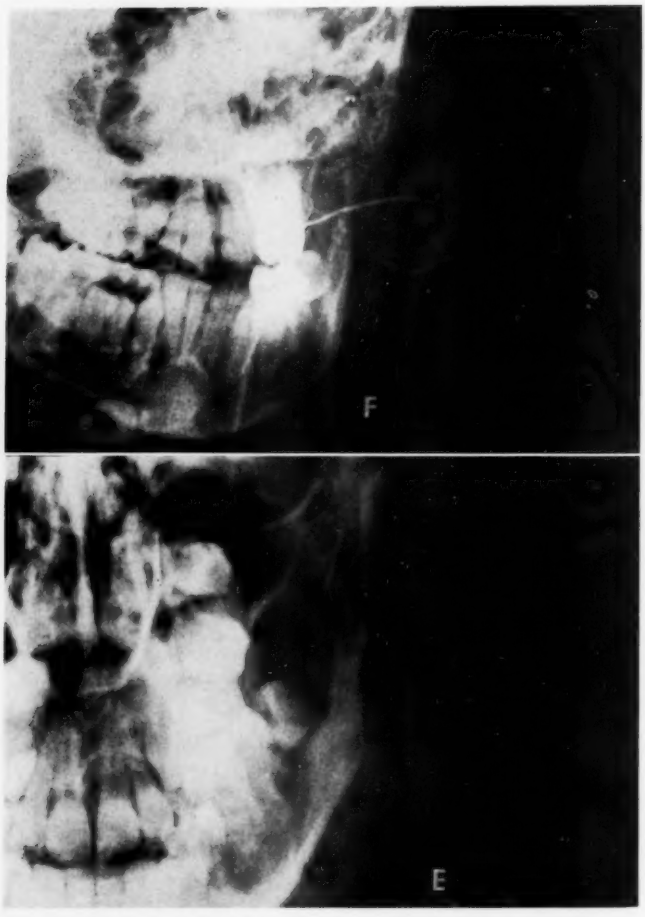


Fig. 5.—Sialogram of case No. 13. There is marked lateral displacement of the entire duct system of the right parotid gland in the filling phase. The general architecture of the duct system is preserved, and there is only slight deviation of the intraglandular ducts with no localizing narrowing or sharp kinking. There is complete evacuation of the contrast material on lemon stimulation. Histologic diagnosis: Traumatic bone cyst of mandible.

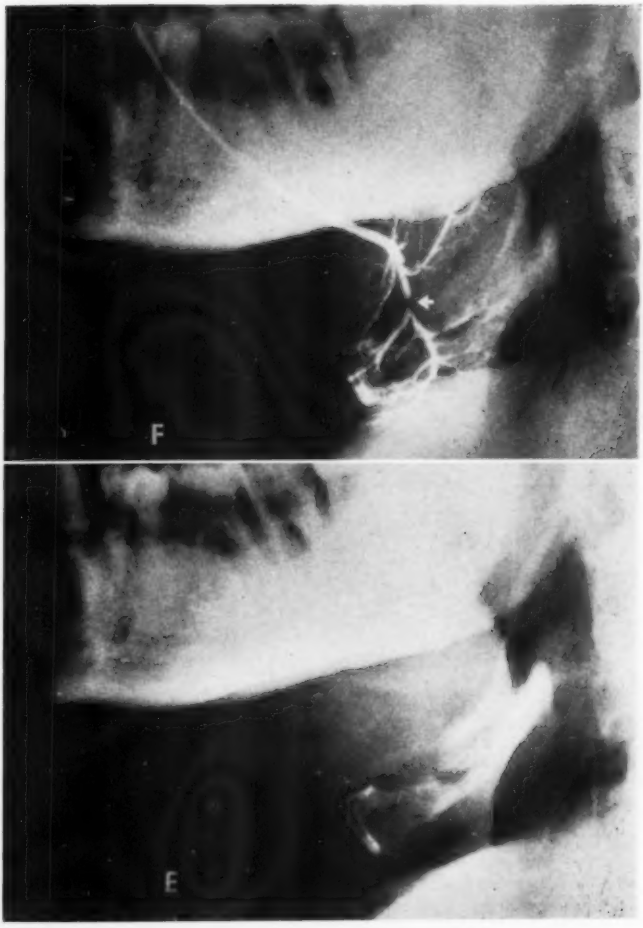


Fig. 6.—Sialogram of case No. 30. Physical examination revealed a 5 x 7 cm mass in the right submaxillary triangle. The filling phase demonstrates upward displacement of the postero-superior secondary ducts with a central localized area of narrowing (arrow). Emptying of the contrast material is complete. At operation there was a huge lymph node compressing the submaxillary salivary gland and indenting it. Histologic diagnosis: Hodgkin's granuloma in a lymph node.

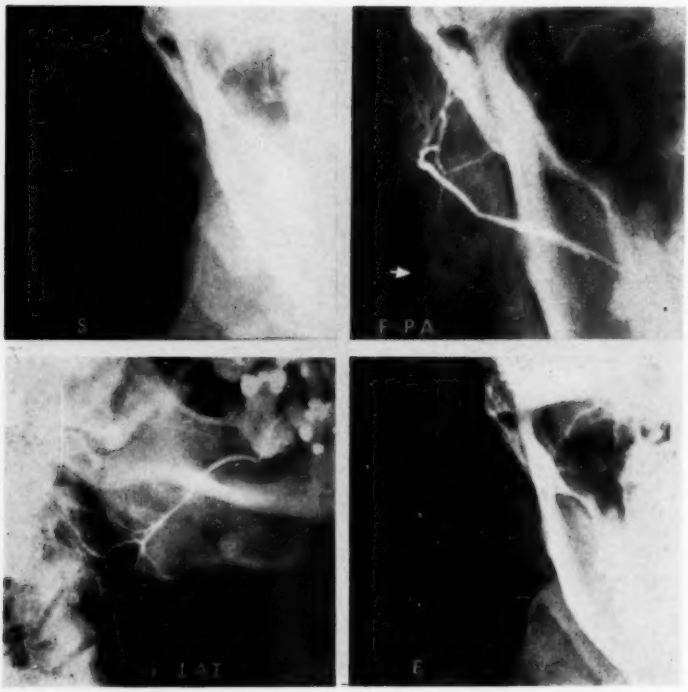


Fig. 7.—Sialogram of case No. 12. Phlebolith of the left cheek, previously diagnosed as a parotid gland calculus. The scout film in the P-A projection shows a 1 cm calcified mass in the "parotid" region, which appears to be located in the inferior portion of the gland, in the filling phase of the parotid sialogram (arrow). However, the lateral projection of the filling phase indicates that the calcified mass is extrinsic and quite anterior to the parotid gland. Emptying of contrast material is complete.

XVI

CHRONIC COMPLETE TRAUMATIC OCCLUSION IN THE LARYNX SECONDARY ENDOTRACHEAL ANESTHESIA AND ITS PLASTIC CORRECTION

DONALD F. PROCTOR, M.D.

AND

MILTON T. EDGERTON, M.D.

BALTIMORE, MD.

Laryngeal complications following endotracheal intubation are likely to be of one of two general kinds. Quite commonly the patient complains of sore throat and mild hoarseness for two or three days following the intubation. Much less frequently (and usually following an excessively prolonged or traumatic intubation) the hoarseness persists and examination reveals a small granulomatous lesion generally located near the posterior end of one vocal cord. Such a lesion can be readily removed through the laryngoscope and the larynx is restored to normal.

The following patient is being reported as an unusually severe complication of endotracheal anesthesia and an interesting problem in the correction of laryngeal stenosis.

REPORT OF A CASE

A white, married female, 31 years of age, first came to our attention in May, 1957. Her complaint was hoarseness and difficult breathing, increasing in severity over a six year period.

The relevant history began in 1951 at which time she underwent a prolonged pelvic operation, in another city, with endotracheal anesthesia. Hoarseness became noticeable shortly afterwards and gradually became more annoying. Three years later, apparently because of the hoarseness, the tonsils were removed under endotracheal anesthesia. No details are available regarding these two operations or the anesthetic techniques employed.

From the Divisions of Laryngology and Otology, and of Plastic Surgery, The Johns Hopkins University School of Medicine.

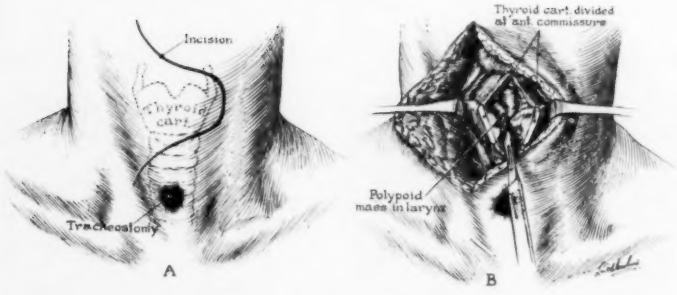


Fig. 1.—The skin incision is indicated in A and the opening of the larynx in B. The cricoid cartilage remains undisturbed.

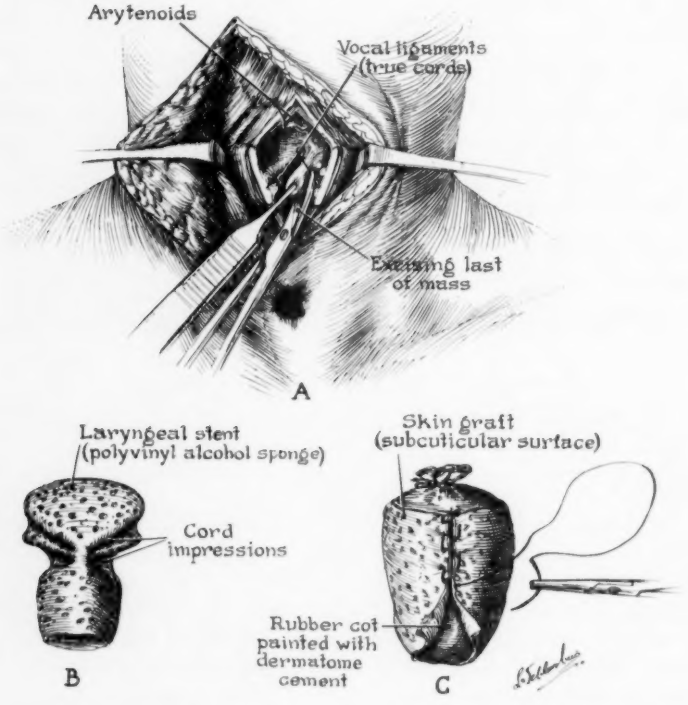


Fig. 2.—Dissection of the granuloma from the underlying muscle is shown in A. The stent and the manner of fixing the skin graft to it are shown in B and C.

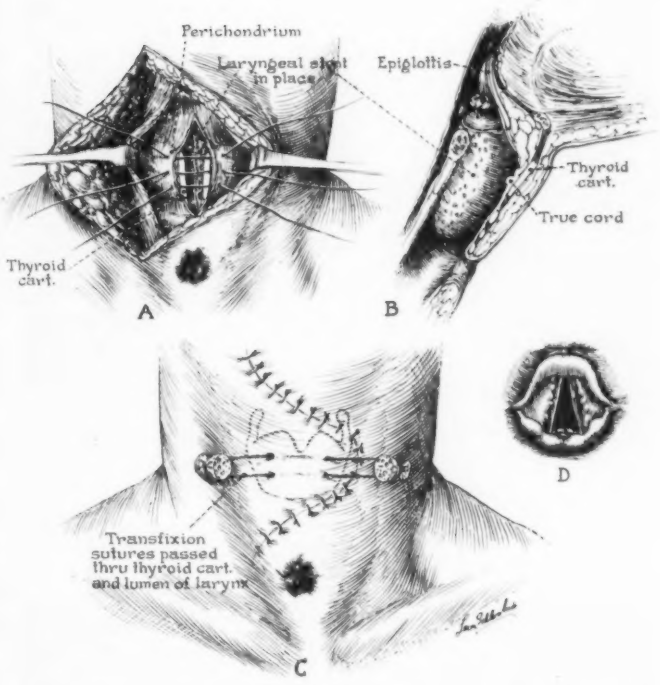


Fig. 3.—Closure of the larynx is illustrated in A, the position of the stent within the larynx in B and the final closure in C. The appearance of the larynx as seen with the laryngeal mirror after full healing is shown in D.

The hoarseness became progressively worse and difficult and noisy breathing began to be severe enough to sharply limit her activities.

By May, 1957, the voice was extremely poor, talking required considerable effort, breathing was difficult at rest, and dyspnea very pronounced on the mildest exertion.

Mirror examination showed the larynx to be nearly filled with a granulomatous mass. The left side of the larynx moved only very slightly on attempts at phonation and motion of the right side was also limited.

On May 16, 1957, after the application of topical anesthesia, an orotracheal tube with an outside diameter of 0.6 cm was forced

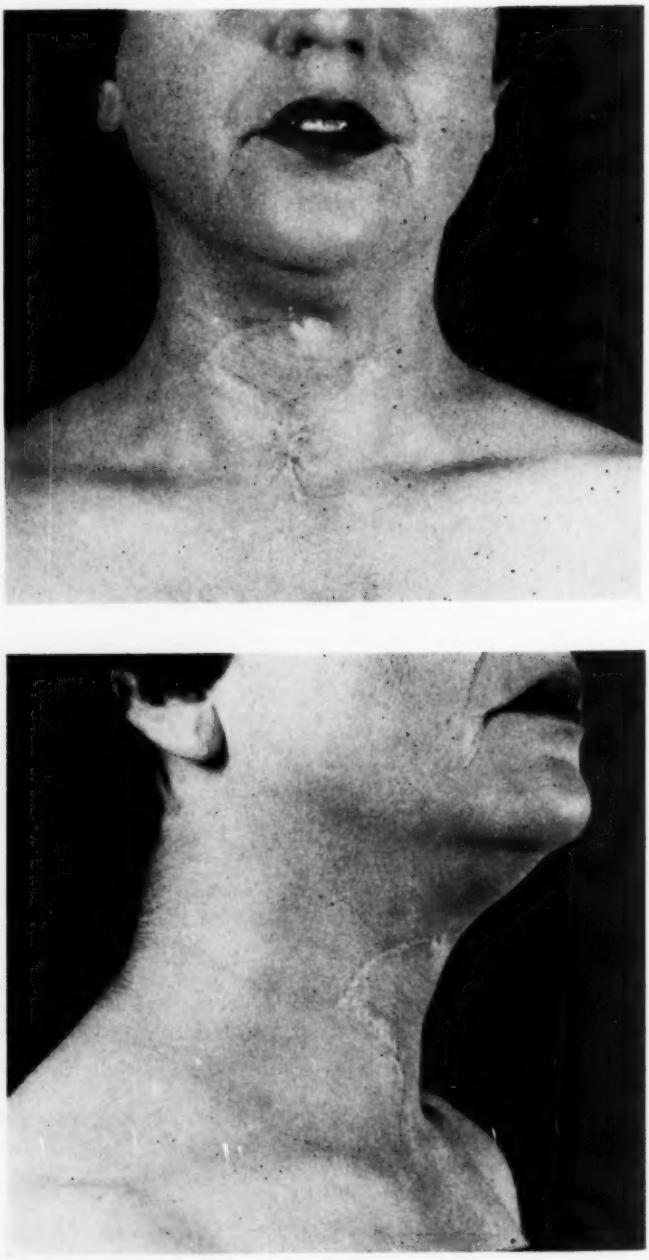


Fig. 4.—Present appearance of the patient.

through the glottic chink with great difficulty. General anesthesia was then induced and a tracheotomy performed. The trachea was opened through the second and third tracheal rings and a tracheotomy tube inserted. The endotracheal tube was then removed and direct laryngoscopy was carried out. It was impossible to make out any normal landmarks below the level of the epiglottis. Tissue was removed for biopsy and showed scarring, granulation tissue, and hyperkeratosis.

Five days later the patient was again given a general anesthetic. A large skin flap was turned back across the midline and the laryngeal cartilages were uncovered. The thyroid cartilage was split down the middle and the larynx entered through the mid anterior line. With this exposure one could see that the entire lining mucosa from the edge of the vocal cords up over the arytenoids posteriorly and to the epiglottis anteriorly was replaced by an irregular granulomatous mass (Fig. 1). This entire mass was removed, chiefly by sharp dissection, down to the underlying muscle. A portion of each arytenoid cartilage was denuded in this process.

A split thickness graft, 0.012 inches thick, was then cut from a hairless area on the anterior chest wall and fitted about a stent of polyvinyl alcohol sponge shaped to fit the normal glottic aperture (Fig. 2). This was held in the denuded portion of the larynx by a No. 28 stainless steel wire suture which passed through the skin and thyroid cartilages. The thyroid cartilages were closed with heavy catgut and the perichondrium and muscle with fine catgut. The skin incision was then closed with subcuticular wire sutures and silk skin sutures. The heavy wire stay suture was fixed to either side of the neck by tying it over a sponge (Fig. 3).

A stomach tube was passed and the patient was placed on tetracycline and penicillin postoperatively. After three days the stomach tube was removed.

By the tenth postoperative day there was some necrosis in the skin margins and one end of the stay suture had eroded through the skin. The silk sutures were removed that day.

On the fifteenth postoperative day, again under general anesthesia, the stay suture was removed and the eroded area of skin was debrided, undermined and closed. The stent was removed through a laryngoscope. It was obvious that the graft had taken nicely and the pale color of squamous epithelium could be easily contrasted with that of surrounding mucosa.

Four days later there was normal motion in the larynx and a good glottic aperture. There was some irregularity along the line where graft met mucosa above. Five days later some granulations were removed from this edge through a laryngoscope.

By June 25, 32 days following surgery, it was apparent that these granulations were steadily increasing. In an effort to interrupt this process the patient was placed on antibiotics and 200 mg of cortisone a day. From this point on there was steady improvement. Five days later the cortisone was reduced to 150 mg a day and a gradual further decrease was carried out. By September 13, just under four months postoperatively, cortisone and antibiotics were stopped.

For the next four months the patient was able to keep the tracheotomy tube corked, and, on January 7, 1958, a secondary closure of the tracheostomy was carried out.

At the present time, ten months after the initial operation, the patient notices no embarrassment to her breathing, and the voice, though hoarse, is quite satisfactorily useful (Fig. 4). There has never been any difficulty with swallowing.

The glottic aperture is approximately two-thirds normal in size. There is a tough fibrous projection from the posterior commissure above the cords (Fig. 3-D).

SUMMARY

1. A serious complication of endotracheal anesthesia is described and illustrated.

2. A method for grafting the lumen of the larynx, including the actual surface of both vocal cords, is described.

3. Postoperative function in this patient has been quite good permitting the removal of the tracheotomy tube and breathing by mouth with acceptable movement of the vocal cords for normal speech and the avoidance of aspiration.

819 Park Ave.

XVII

AUDITORY SENSITIVITY AND THE MAGNITUDE OF THE COCHLEAR POTENTIAL

THOMAS E. MCGILL, PH.D.

WILLIAMSTOWN, MASS.

The electrical theory of auditory nerve stimulation, as presented by Wever,[19] has gained wide acceptance among acoustic scientists in recent years.[3,6,9,16] The electrical theory may be stated quite simply. Under acoustic stimulation the hair cells of the cochlea produce a pulsating direct-current, called the cochlear potential, which triggers the fibers of the auditory nerve. The cochlear potential is thus a response to acoustic stimulation and, at the same time, a stimulus for the auditory nerve.

In the chain of events leading to hearing factors both preceding and following the cochlear potential affect sensitivity. Precochlear potential factors, e.g., the condition of the middle ear mechanism, must affect sensitivity by means of their effect on the cochlear potential. The magnitude of the potential, in turn, reflects the condition of that part of the acoustic system which precedes it. On the other hand, the cochlear potential reflects nothing of the state of the acoustic system beyond it. The auditory system can thus be viewed as neatly divided into two parts by the cochlear potential; as Boring put it, a measurement of the cochlear potential ". . . taps the chain of causal events at the cochlea and before the nerve."[2]

Using the above model, provided by the electrical theory of auditory nerve stimulation, the present study was designed in an attempt to answer two questions.

1. What is the magnitude of the cochlear potential at the threshold of hearing and how does the magnitude relate to frequency?

This paper is based on a dissertation presented to the Department of Psychology of Princeton University in partial fulfillment of the requirements for the Ph.D. degree. The author is grateful to Professors Wever, Rahm, Vernon, and Strother for their guidance and assistance in this research. The research was supported by contract Nonr-1858(18) between the Office of Naval Research and Princeton University. Reproduction in whole or in part is permitted for any purpose by the U.S. government.

2. With what success may we predict from differences in behavioral sensitivity (from animal to animal) to the relative magnitudes of the cochlear potential?

Answering question two is, in effect, testing the electrical theory of auditory nerve stimulation. If the cochlear potential is in fact the neural stimulus, then certain relationships should hold between behavioral-sensitivity differences and the magnitude of the potential. These relationships should be such that a more sensitive animal (behaviorally) generally produces (a) a cochlear potential of greater magnitude for a given sound-intensity and (b) a cochlear potential of lesser magnitude for threshold sound-intensity, than a less sensitive animal produces. Clause (a) follows from a consideration of the cochlear potential as a response of the first part of the acoustic mechanism. It has been repeatedly demonstrated (see especially reference 21) that experimental manipulations which are known to reduce auditory sensitivity also reduce the magnitude of the potential. Therefore, it is to be expected that a more sensitive animal will generally exhibit a cochlear potential of greater magnitude than a less sensitive animal to a given sound-intensity. Clause (b) follows from a consideration of the cochlear potential as the stimulus for the auditory nerve. By definition a more sensitive animal requires a stimulus of less intensity to reach threshold than that required by a less sensitive animal. Therefore, the cochlear potential exhibited by a more sensitive animal for a sound intensity representing his behavioral threshold should generally be of lesser magnitude than the potential exhibited by a less sensitive animal for his behavioral-threshold sound-intensity.

The modifier "generally" in the above statements requires a word of explanation. Since both pre- and postcochlear potential factors affect sensitivity and a cochlear potential measurement reflects only one set of factors, the relationship expressed is not necessarily perfect. For example, it is entirely possible for an animal to exhibit a cochlear potential of relatively great magnitude and at the same time to be relatively deaf due to neurological factors. However, if the assumption is made that such cases are randomly distributed within the population, then the relationship should remain positive.

APPARATUS AND METHODS

Subjects (*Ss*). The subjects were four cats whose sex and age in months at final threshold determination were as follows: F-10, F-13, M-24, M-30.

Training Apparatus and Methods. The experiment was conducted in two soundproof rooms (116 inches high x 118 inches long x 70 inches wide) which were joined by means of double doors. The experimenter (E) and all sound producing apparatus except the speakers were located in one room and the training box was located in the other room. Observation was by means of a one-way mirror between the rooms and a piece of plate glass set in the wall of the training box.

A General Radio beat frequency oscillator type 1304A was the major component of the sound producing apparatus. The output of the oscillator was led into an onset generator which permitted variation in the onset and decay time of the tones. A one-half second onset and decay time was used to eliminate transients and clicks. The output of the onset generator led into an attenuator which permitted intensity variations of 1 db. From the attenuator the signal passed through an 8-ohm impedance-matching transformer into nine Jensen type P6-T 6 inch speakers wired in series-parallel in an arrangement which held phase variations to a minimum.

An elaborate training box was constructed in an attempt to hold sound-pressure-level variations to a minimum. Briefly described, the box was 9 feet long, 2 feet wide, and 2 feet high, covered with two inches of plaster, with the speakers mounted on one end in such a manner that a plane wave sound-front passed through the training area and was absorbed by a series of curtains hung within the box.

The training area itself consisted of a space within the training box 30 inches long, 20 inches high, and 20 inches wide. A piece of half-inch hardware cloth, 6 inches high and 20 inches long, was attached to the floor across the training area. This fence divided the area into two equal parts (15 inches x 20 inches x 20 inches). The part nearest the speakers was designated the "reinforcement side" and the part farthest from the speakers was designated the "waiting side."

The animals were trained, by the method of successive approximations,[8] to sit down on the waiting side facing the speakers. At the presentation of the tone they crossed the six-inch fence and a piece of food was dropped through the ceiling of the reinforcement side into a shallow metal dish. After eating, Ss returned to the waiting side, sat down, and awaited the next trail. The food drop was accomplished by means of a conveyor belt mounted on top of the training box and mechanically operated by E from the other room.

After Ss had been trained to wait up to four minutes, audiogram determination was begun. The up-and-down method as described by Guilford[7] was used. The efficiency of this method for audiometric threshold determinations has been established.[13] The mean of four threshold determinations taken for each frequency at each session was considered the threshold for that session. The unit by which the intensity of the stimulus was manipulated was progressively decreased until the final unit-value of 3 db was reached. The order of frequency presentation from session to session was randomized and the time between trails was varied from ten seconds to four minutes. The tone remained on for 12 seconds or until the animal had responded and the food had dropped.

The problem of deciding at what point learning had ceased and a true measure of the absolute threshold had been obtained was met by adopting a three-part criterion.

1. The threshold range of eight consecutive sessions at any frequency had to be within 6 db.

2. The mean of the last four thresholds could not demonstrate more than one db improvement in sensitivity over the mean of the first four sessions.

3. The last threshold determination could not be lower than the other seven.

Variations in sound pressure level were measured using a Western Electric type 640AA condenser microphone and probe tube. The output of the microphone was amplified and fed into a General Radio Wave Analyzer type 736-A which was operated as a narrow band-pass voltmeter. The entire area in which it was possible for S to place his head during presentation of the stimulus was probed.

Cochlear Potential Recording. After the final threshold determination had been made Ss' ears were operated upon,[21] and cochlear potentials were recorded from the round windows. The two-hole technique, as described by Rahm, Strother, and Crump,[12] was used. The active electrode, which was placed in contact with the round window, consisted of a nylon coated copper wire (0.13 mm diameter) to the end of which was soldered a triangularly shaped piece of platinum foil, 2.5 micra in thickness, with an altitude of 3 mm and a base of 1 mm. A steel hypodermic needle inserted into the superficial layer of the masseter muscle served as the inactive electrode. Coch-

lar potentials picked up from the round window were amplified and fed into a General Radio Wave Analyzer type 736-A which was operated as a narrow band-pass voltmeter.

The operating room was soundproof and electrically shielded. The subjects remained in this room during cochlear potential recording. The sound producing apparatus consisted of two oscillators, one of which had a fixed frequency of 50,000 cps. The second was variable from 34,000 to 50,000 cps, thus giving the apparatus a frequency range of from 1 to 16,000 cps. The signal from each of these oscillators went to a detector whose output was connected through a filter and an amplifier to a Davan attenuator (type T-690 CR). Output from the attenuator fed into a power amplifier which drove the speaker (Western Electric 555 receiver). The aerial sound produced by the speaker was conducted into the operating room by a tube.

The animal was placed on the operating table so that the open end of the sound tube was two inches from the pinna. The head was oriented in such a manner that a straight line from the center of the sound tube opening would have entered the external auditory meatus. The probe of the condenser microphone was then passed by the edge of the pinna, just touching it. The opening of the probe was placed so as to just intersect (perpendicularly) the imaginary straight line from the center of the sound tube. The microphone was used to measure the sound pressure level of the stimulus.

Cochlear potentials were then recorded for the 11 frequencies. The magnitude of the potentials were then recorded for the 11 frequencies. The magnitude of the potentials was recorded at as low a level as the apparatus and the physiological noise level of the preparation permitted (generally about 0.5 microvolt). The upper level of recorded magnitude was kept well within the limits of linearity.[20]

RESULTS

Behavioral Results. The ranges of sound pressure variations for the 11 frequencies, as measured in the waiting side of the training area, were as follows:

100 cps	2 db	1,900 cps	11 db
200	4	2,900	8
290	7	5,200	9
500	9	6,800	8
700	10	10,000	7
1,000	10		

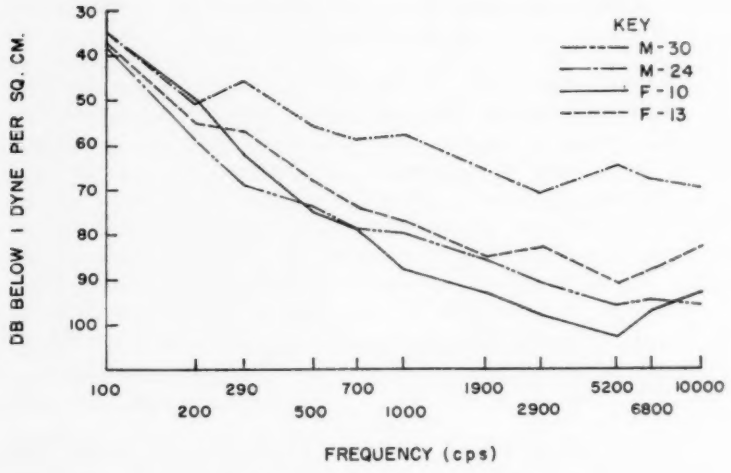


Fig. 1.—Individual cat audiograms.

The maximum sound pressure level observed at each frequency was used in computing the thresholds. As Neff and Hind[11] pointed out, this procedure reflects the least sensitivity of which the animals are capable. On the other hand, as Dworkin et al[5] have noted, at near threshold intensities the animals actively sample the sound field by moving their heads about in it. For these reasons the maxima seemed the best estimate for stimulus specification purposes.

Figure 1 presents the means of the eight threshold determinations for each animal at each frequency.

Neff and Hind have recently carried out a study of auditory sensitivity in the cat in which a pure-tone audiogram was established for the frequency range of 62.5 cps to 60,000 cps. As Neff and Hind noted, their audiogram was the first reported for the cat which used direct measures of the sound pressure level. Earlier studies[5,18] had made use of indirect measures, such as electrical input to a sound source, for the purpose of stimulus specification.

Figure 2 presents the cat audiogram as determined by Neff and Hind, a human audiogram, and the mean audiogram for the three most sensitive cats from the present study. Animal M-24 was not included because of his relatively high thresholds (Fig. 1). The

two cat audiograms show good agreement when compared with the various human curves available.[10] There are reasons, however, why the procedures employed in the present study might be expected to result in lower thresholds than those reported by Neff and Hind. In the present study the animals were young, a stringent learning criterion was employed, the stimulus remained on three times longer (12 sec as compared to 4 sec), and a smaller intensity unit was used (3 db as compared to 5 db). Probably the most important difference between the two studies was in the type of reinforcement used. The conditioned avoidance technique which Neff and Hind used presents certain difficulties near threshold. If the animal does not respond, E is left with the decision of whether or not to apply shock. If S heard the tone and no shock is given, the response may begin to extinguish. If the animal did not hear the tone and shock is given, spontaneous responses increase. Concerning this problem Neff and Hind wrote: "Particular care was taken in the present experiment to force each animal to respond at the limit of its ability but at the same time to avoid eliciting spontaneous responses which are likely to occur when an animal is punished often for failing to respond to tones below or near threshold.[11]" This problem does not arise in positive-reinforcement situations where the reinforcement is only delivered after the appropriate response has occurred.

Cochlear Potential Results. Subject M-24 displayed insensitivity to auditory stimuli (Fig. 1) and the operation revealed a progressive infection of both ears. The cochlear potentials were of low magnitude; drifts and jumps in magnitude made the response non-reproducible. For this reason the data from M-24 are not included in the results which follow.

The collected cochlear potential data were treated in the following manner. For each ear the data collected at each frequency were plotted on double-logarithmic co-ordinates. All functions were linear and none showed enough variation in slope to change the rank-order among Ss. The results presented for M-30 represent data on the right ear only. The left ear of M-30 displayed the same clinical picture that both ears of M-24 had displayed. The results for Ss F-10 and F-13 represent the mean of their two ears. Both of these animals had ears which were closely similar to one another.

Figure 3 represents the cochlear potential magnitudes which resulted when a given sound intensity was introduced into the ears of the three Ss. In some cases it was not considered safe to stimulate the ear with an intensity of one dyne so that a portion of Figure 3 was extrapolated from functions recorded at lower intensity levels.

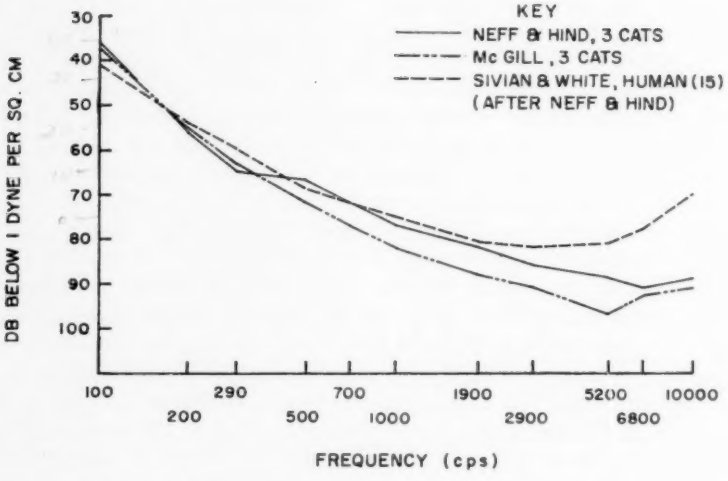


Fig. 2.—Audiograms. Two groups of cats and one group of humans.

The magnitude of the cochlear potentials could not be directly measured for threshold stimulation. The limitations of the equipment and the physiological noise-level of the preparation prevented this measurement. The cochlear potential magnitudes at threshold presented in Figure 4 were determined by linear extrapolation from the functions recorded at higher intensities. There are good reasons for faith in the exactness of the results of this procedure. The function of the recorded potentials is linear to the lowest intensities at which it is possible to make measurements; killing the animal, and thus reducing the physiological noise-level, at once permits recording at a level ten times lower[21] and the function still appears linear. The best estimate, then, of the magnitude of the cochlear potential at a low intensity is a direct linear extrapolation from that portion of the function recorded at higher intensities.

Figure 5 presents the means of the cochlear potential magnitudes at threshold for the three cats.

Data Analysis. In order to test the predictability of the electrical theory the data were treated in the following manner. First, a search was made for statistically significant differences in the behavioral thresholds. At each frequency the eight threshold determina-

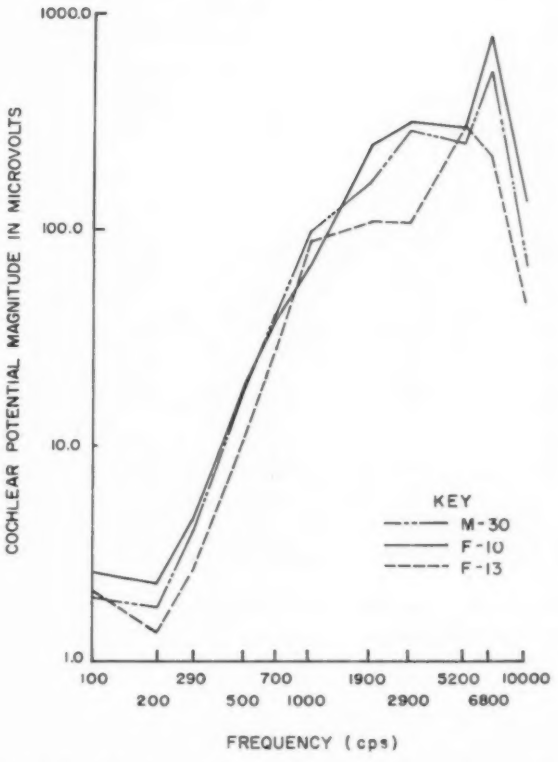


Fig. 3.—Equal-intensity curves. The ordinate shows the magnitude of the cochlear potential for a standard sound-intensity of one dyne per sq cm.

tions for a given cat were tested against the determinations for the other two cats. The Wilcoxon Paired Replicates test[22] was used. Of the 33 possible comparisons, 28 revealed statistically significant differences; two at the .05 level, one at the .02 level, and 25 at the .01 level.

The statement concerning relationships put forth under question number two in the introduction was then tested as follows. The 28 significant differences in behavioral threshold were used as predictors of rank-order differences in cochlear potential magnitude. Figure 3 was used to test clause (a) of the relationship statement: a more sensitive animal generally produces a cochlear potential of greater magnitude for a given sound-intensity. Figure 4 was used to test clause (b)

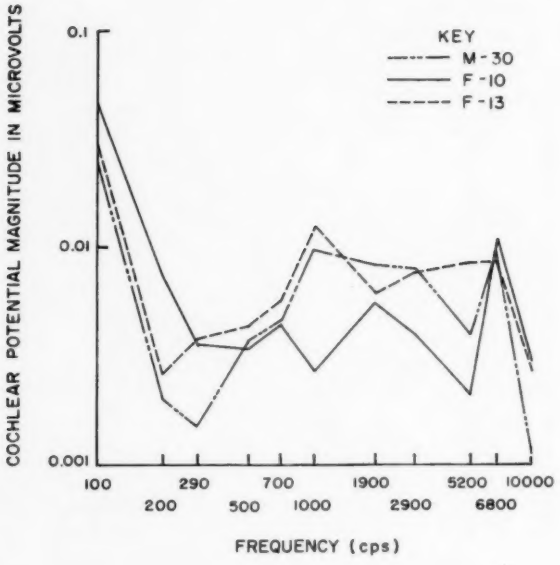


Fig. 4.—The magnitude of the cochlear potential at the threshold of hearing. Individual curves.

of the relationship statement: a more sensitive animal generally produces a cochlear potential of lesser magnitude for threshold sound-intensity. Each difference in rank-order correctly predicted by the electrical theory was scored with a plus; each incorrect prediction was scored with a minus. Siegal's sign test with continuity correction[14] was used to test the significance of the predictions. The null hypothesis of a chance prediction was rejected at the .02 level in the case of Figure 3 and at the .01 level in the case of Figure 4. In other words, the electrical theory has predicted from behavioral-sensitivity differences to rank-order differences in the magnitude of the cochlear potential with above-chance success.

COMMENT

What is the magnitude of the cochlear potential at the threshold of hearing and how does the magnitude relate to frequency?

The answer to this question, as provided by the data presented in Figure 5, is relative to the procedures used in the present study.

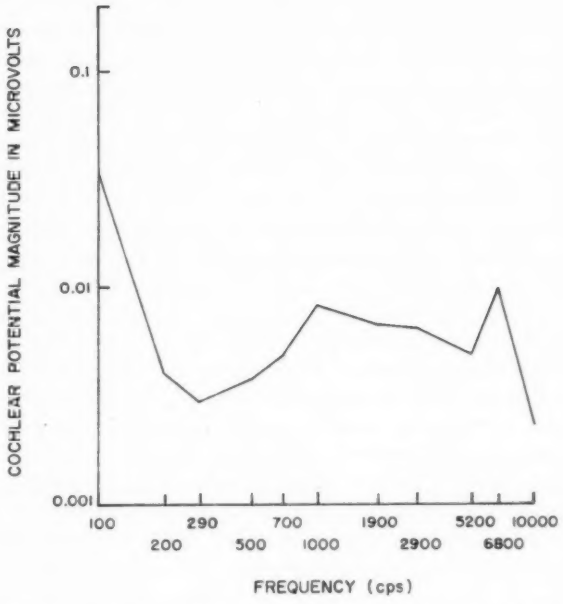


Fig. 5.—The magnitude of the cochlear potential at the threshold of hearing. Mean-data from Figure 4.

For example, the choice of the position of the active electrode affected the results. As Wever and Lawrence have shown,[21] the potentials recorded at the round window exceed those recorded at the apex of the cochlea by an amount which varies with frequency. Thus any change from the round window site would probably raise most of the points in Figure 5 to some higher value and, at the same time, change the shape of the function.

According to the electrical theory of auditory-nerve stimulation, Figure 5 represents the minimum adequate stimulus for the neural processes, as recorded from the round window. The magnitude of the potential at the actual site of stimulation, i.e., at the nerve fibers, is undoubtedly greater than that recorded from the round window since the potential has been attenuated by the cochlear fluids. Estimates of this attenuation vary,[4,17,21] but there is agreement that it is considerable.

With the above fact concerning attenuation in view, it at first seems strange that 10,000 cps should have such a low value. It has

been repeatedly demonstrated that high tones exhibit maximum amplitude of basilar-membrane displacement in the base of the cochlea. For tones lower in frequency the maximum moves toward the apex. Thus, the round-window position probably offers a truer picture of the actual cochlear potential magnitude for a 10,000 cps tone than it does for a tone lower in frequency. Since the fluid pathways to the round window are relatively short for 10,000 cps, the attenuation must be correspondingly less and the expectation might be of a relatively large cochlear potential. Another factor which must be considered, however, is the relative spread of the response in the cochlea. A general statement of this relative spread is that it is large for low-frequency tones and small for high-frequency tones. For 10,000 cps, then, the spread of effective activity is small relative to the other frequencies used. Therefore the energy is concentrated over a smaller area of the basilar membrane. The low value exhibited by the high tones was anticipated by Wever who wrote: "A sound attains threshold loudness, we suppose, when it excites some minimum number of nerve impulses, and its success in doing so depends not only on the amount of energy applied but on the distribution of that energy. Because nerve fibers have a threshold below which excitation is wholly ineffective it is more advantageous, when the quantity of energy is small, to focus it on only a few elements rather than to spread it over a great many. The high tones, for which the stimulus action is relatively concentrated, secure an advantage on this account."[19]

This position is supported by the gradual decline in magnitude from 1,000 cps to 10,000 cps, with the exception of 6,800 cps. The value for 6,800 cps appears aberrant. Reference to Figure 4 reveals that two of the three animals showed a sudden change in direction for this frequency. The writer has no explanation to offer as to why such a shift occurred; it is simply suspected that the 6,800 cps point represents some sort of aberration and that the actual value should be six or seven db less than that depicted.

The high values resulting for the low frequencies are attributable to a different factor. At low frequencies a relatively large neural component is present in the cochlear potential recording due to a great number of nerve fibers firing in phase. As frequency is raised the number of neurons firing per cycle is reduced, and the neural component grows smaller.

With what success may we predict from behavioral-sensitivity differences (from animal to animal) to the relative magnitudes of the cochlear potential?

The answer to this question is that we may predict with better than chance success. A general statement of the relationship discovered is that which is predicted by the electrical theory of auditory nerve stimulation and may be phrased as follows: if animal A is more sensitive than animal B for a given frequency, it is probable that animal A exhibits a cochlear potential of greater magnitude for a common sound-intensity, and a cochlear potential of lesser magnitude for threshold sound-intensity, than animal B exhibits.

The sort of predictability test employed in the present study cannot prove the electrical theory if it succeeds, but it can question it if it fails. Because of the narrow limits within which the theory successfully operated, the results are interpreted as strong support for the electrical theory. It is difficult to conceive of the cochlear potential reflecting so accurately the action of the neural stimulus without actually being the neural stimulus.

In 1951 Ash wrote, "The precise relationship of cochlear response levels to acuity threshold levels is not yet clear."[1] It is felt that, although much work may be needed to determine the precise relationship, the present study has established the general relationship.

SUMMARY

This study was designed to determine the magnitude of the cochlear potential at the threshold of hearing and its relation to frequency, and to test the electrical theory of auditory nerve stimulation through predictions from behavioral-sensitivity differences to the relative magnitudes of the cochlear potential.

Audiograms were determined for a group of cats using 11 frequencies in the range of 100 cps to 10,000 cps. The animals were trained to cross a barrier for food at the sounding of a tone. Following audiogram determinations, the ears of the animals were operated upon and cochlear potentials were recorded from the round windows.

The major findings were as follows:

1. The magnitude of the cochlear potential for behavioral-threshold sound-pressure levels was determined and its relationship to frequency was presented and discussed.

2. Predictions from behavioral-sensitivity differences to differences in cochlear potential magnitudes can be made with better than chance success. The following general relationships were determined:

a. A more sensitive animal generally produces a cochlear potential of greater magnitude for a given sound-pressure level than a less sensitive animal produces.

b. A more sensitive animal generally produces a cochlear potential of lesser magnitude for behavioral-threshold sound-pressure level than a less sensitive animal produces.

3. One animal exhibited very high behavioral thresholds. The operation disclosed infections of both ears and the resulting cochlear potentials were of low magnitude and unreliable.

4. The data support the electrical theory of auditory nerve stimulation.

WILLIAMS COLLEGE, DEPT. OF PSYCHOLOGY

REFERENCES

1. Ash, P.: The Sensory Capacities of Infrahuman Mammals: Vision, Audition, Gustation. Psychol. Bull. 48:289-326, 1951.

2. Boring, E. G.: Sensation and Perception in the History of Experimental Psychology. New York: Appleton-Century, 1942.

3. Davis, H.: The Bio-Physics and Physiology of the Inner Ear. Physiol. Revs. 37:1-49, 1957.

4. Davis, H., Gernandt, B. F., Riesco-MacClure, J. S., and Covell, W. P.: Aural Microphonics in the Cochlea of the Guinea Pig. J. Acoustic Soc. Amer. 21: 502-510, 1949.

5. Dworkin, S., Katzman, J., Hutchinson, G. A., and McCabe, J. R.: Hearing Acuity of Animals as Measured by Conditioning Methods. J. Exp. Psychol. 26:281-298, 1940.

6. Granit, R.: Receptors and Sensory Perception. New Haven: Yale University Press, 1955.

7. Guilford, J. P.: Psychometric Methods. (2nd Ed.), New York: McGraw-Hill, 1954.

8. Hilgard, E. R.: Methods and Procedures in the Study of Learning. In S. S. Stevens (Ed.), Handbook of Experimental Psychology. New York: Wiley, pp. 517-567, 1951.

9. Lawrence, M.: Hearing. Annu. Rev. Psychol. 8:29-60, 1957.

10. Licklider, J. C. R.: Basic Correlates of the Auditory Stimulus. In S. S. Stevens (Ed.), Handbook of Experimental Psychology. New York: Wiley, pp. 985-1039, 1951.

11. Neff, W. D., and Hind, J. E.: Auditory Thresholds in the Cat. J. Acoustic. Soc. Amer. 27:481-483, 1955.

12. Rahm, W. E., Jr., Strother, W. F., and Crump, J. F.: The Effects of Pressure in the External Auditory Meatus. ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY 65:656-664, 1956.

13. Seiden, H. R.: Auditory Acuity in the Marmoset Monkey. Unpublished doctoral dissertation, Princeton University, 1957.

14. Siegel, S.: Nonparametric Statistics for the Behavioral Sciences. New York: McGraw Hill, 1956.

15. Sivian, L. J., and White, S. D.: On Minimum Audible Sound Fields. J Acoustic Soc. Amer. 4:288-321, 1933.

16. Tasaki, I.: Hearing. Annu. Rev. Physiol. 19:417-438, 1957.

17. Tasaki, I., and Fernandez, C.: Modifications of Cochlear Microphonics and Action Potentials by KCI Solution and by Direct Currents. J. Neurophysiol. 15: 497-512, 1952.

18. Wever, E. G.: The Upper Limit of Hearing in the Cat. J. Comp. Psychol. 10:221-233, 1930.

19. Wever, E. G.: Theory of Hearing. New York: Wiley, 1949.

20. Wever, E. G., and Lawrence, M.: The Patterns of Response in the Cochlea. J. Acoustic Soc. Amer. 21:127-134, 1949.

21. Wever, E. G., and Lawrence, M.: Physiological Acoustics. Princeton, N. J.: Princeton University Press, 1954.

22. Wilcoxen, F.: Some Rapid Approximate Statistical Procedures. New York: American Cyanamid Company, 1949.

XVIII

FACIAL KINETOGRAPH

A DESCRIPTION OF A METHOD FOR THE STUDY OF NEW TREATMENTS FOR FACIAL PARALYSIS

AUGUST L. STEMMER, M.D.

BOSTON, MASS.

A universally acceptable method that permits scientifically accurate graphic representation of facial function over prolonged intervals of time is worthy of attention as it is a basis for all therapeutic programs in any type of facial paralysis. The following method has been chosen because of its simplicity, ease of adaptation, and accessibility within the usual hospital facilities. The facial kinetograph is a radiographic instrument for demonstrating and recording early clinically recognizable changes in facial muscular movement. This method is to be considered on a separate basis from the electromyographic methods now available to the physiotherapist and the physiologist; that is to say, the earliest detection of the electromuscular activity does not fall within the realm of facial kinetography whose job it is to record the percentage of return to normal muscular function in a given period of time.

A review of the literature under the headings: 1) facial: a. expression; b. paralysis; c. radiographic movement; 2) muscular movement: a. contraction; b. movement; c. radiography; 3) paralysis: a. facial, has failed to disclose a simpled method. The articles which could not be obtained are so listed in the references.

Clinically recognizable, gross facial movement is still the final basis for the evaluation of facial nerve function.

Most of the attempts at depicting gross facial movement center around photography. Hayes Martin[1] superimposes one photograph upon another, thus allowing for a comparison of changes over a period of time. Others have used motion pictures. Although good, these methods have shortcomings in determining end points and in con-

From the Department of Otolaryngology, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts.

fusion which arises from extraneous detail such as hair arrangement, weight, etc. Bony reference points are constant whether the patient has gained weight or not.

It is an easy matter to affix a small lead marker to the labial commissures and record their movement when the patient smiles during the roentgen ray exposure of an x-ray film. By comparing the abnormal with the normal side, after correcting for "skew," one is able to arrive at a measure of function during any period of time (Fig. 1).

MATERIALS

At first, small sections of paper clips were utilized. Next, small pieces of lead shot were attached with collodion to the face. The usual radiographic equipment, utilized in sinus films, was all that was necessary to produce easily interpretable results. To further study these results, a heavy piece of lead soldering wire was bent into the shape of a jaw, and was swung in front of an x-ray plate and exposed at various angles, to judge the amount of distortion or "skew" that one could expect in moving the chin in extreme positions off of the midline. A head holder can be worked out so that each patient may be placed in successively identical positions at different times, for an easier interpretation of the findings. However, this is not necessary and it becomes clear that with a simple knowledge of the types of distortion one can readily come to a reasonably accurate determination.

TECHNIQUE

The patient is seated in front of the x-ray cone with his head tilted forward (Fig. 2) at an angle of approximately 30 degrees, so that the lead shot placed at the commissures will be readily differentiated from metal fillings in the patient's teeth, which may lie in juxtaposition. He is then told to smile and to relax on the 1-2 count; one, smile; two, relax; allowing one second second for the height of the smile and one second back to normal. Thus, a two-second exposure is practical and there is little bony movement to obscure interpretations. The dried film is then placed on an x-ray viewing box and lines can be drawn to show the outermost extremes of movement on both sides.

To estimate the amount of skew, one selects a center point which can be readily used for reference, such as the contact point between the two lower central incisors, or the genial tubercule of the mandible,

Figure 1

along with the right and left lingula mandibulari, or the condylar heads. A line is then drawn connecting these points on each side, forming a "V". If the "V" is in a central position, interpretation can be considered within the limit of error of the investigator's ability to measure approximately ¼ mm to ½ mm with mechanical drawing instruments. If the "V" is falling on its side with elongation of one of its legs, one must consider that foreshortening exists and the per cent of error can be calculated (Fig. 4).

The true vector relationships involved in actual calculation of percentage error are rather complex for general clinical use and they do not seem necessary for the gross observation intended. Better corrections of the geometric error may be evolved; however the following assumptions seem useful at this stage, since they reflect the complexities of the three dimensional geometric problem which has not been perfected as yet:

1. The longer leg of the "V" is erroneous since a more accurate interpretation depends on less elongation of the mandibule at the

Figure 2

expense of possible confusion between markers and fillings as mentioned under the above method earlier.

2. If the film margins are in such a manner as to be horizontal and parallel with the floor and ceiling, then for proper results, both legs of the "V" are of equal length, with its apex at the center, hanging like a plum line.

3. Since the radiograph has the unique ability to disassociate the horizontal and vertical planes,, if the right and left side are dependent upon each other for their gross movements (i.e., both labial commissures move with chin), then notable skew might be more likely to exist when the chin is moved both sideways and down at the same time. Vertical and horizontal apparent skew, i.e., as it appears to be on the film, if able to cause error could do so singly or in combination

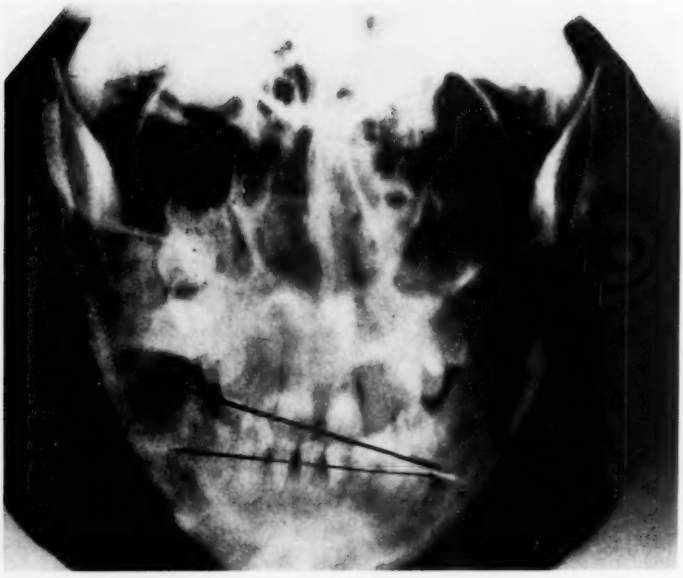


Figure 3

since interpretation is dependent upon a complex interrelationship of variable smile vectors to each other and to their position in space. Therefore, despite the fact that similar measurements of leg length, etc., could give a more accurate correction of the actual complexities of all of the vectors involved, at present, a selection of a central axis seems to more clearly represent the central idea that many vectors are concerned—none of which have been accurately analyzed. Justification of such an approach lies only in the fact that to undertake a complex vector analysis study would prolong the time in which the method would be tested on large groups; possibly at the expense of finding the geometric errors nearly negligible in comparison to those lying within other shortcomings of this method.

Using a compass and straight edge, by utilizing the free margin of the x-ray film (since it was placed at a true vertical with the patient) one draws a horizontal, level with the shortest leg of the "V". The length of the apex (true axis) is measured from the horizontal line just drawn and is considered the true commissural movement. The erroneously elongated leg is then geometrically reconstructed by

Figure 4

placing it upon this horizontal line without changing the distance of this inverted triangle's base. Again, a vertical axis is obtained, this time corrected for the new triangle's horizontal base. One then considers that the labial commissural movement on the side of the elongated leg was foreshortened by the percentage of elongation of the corrected vertical axis if the axes are separated by greater than approximately 4 mm.

Final interpretation can be made in terms of normal movement such that if the paralyzed side shows a length between markers of approximately one-half that of the normal side, one can, simply, and despite obvious liberties with interpretation, come to a reasonable conclusion that there has been approximately a 50 per cent loss of facial movement on the affected side.

When one's method is perfected, he may find that if the actual elongation of one leg is less than 4 mm, there is no need to figure the error since it is less than two per cent which is less than that consistent with the abilities of most investigators to estimate fractions of a mm.

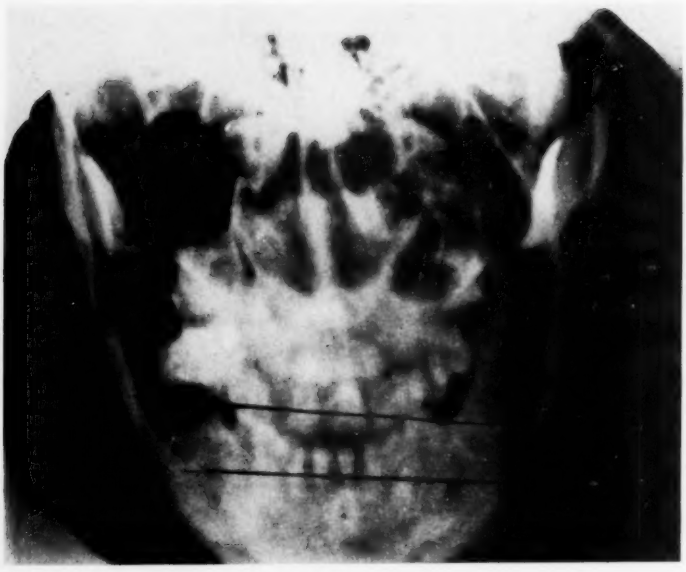


Figure 5

RESULTS

As a pilot study in an effort to determine the likelihood of error, the lead solder reconstruction of a jaw, mentioned earlier, was made, and this was moved into various positions. It was found that a downward and sideways tilt of several centimeters was necessary before readily measurable error could be produced. This was found to be directly related to the horizontal axis, as previously described, and dependent on the interrelation of both movements.

Thirty-five normal facial kinetographs were obtained, utilizing a rough gross segment of age groups between 18 and 65. A difference of commissural movement from the left side to the right between 0 and 2¾ mm was discovered. The percentage of error ranged as high as 16.0 per cent in only one case, despite the use of a headholding device. This allows for a rough interpretation of the error of method in the category of approximately 2 mm, and since the general average was slightly less than 20 mm, one may estimate that an error of approximately 10 per cent lies in the methods of measurement, interpretation, and actual differences in the smile of normal individuals.

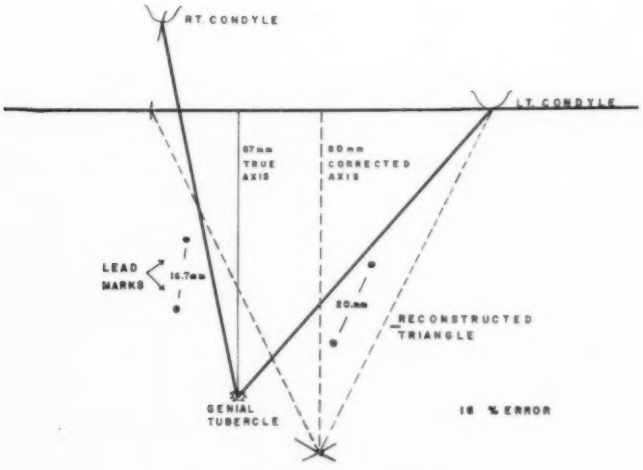


Fig. 6.—Correcting for skew.

The amount of actual distortion of the image is small, due to the large difference in object-to-film distance since the x-ray tube is placed at a distance of some three to four feet from the film while the labial commissures are approximately five inches from the film. The end points are considered as the discernible extent of movement; therefore, some error lies in interpretation of the furthermost extent of the blur which is clear or vague depending upon smoothness or jerkiness of the facial movement.

Of those patients studied for facial paralysis, the case of H. E. is of interest in that this individual had a facial kinetograph taken immediately at the outset of his facial paralysis due to otitis media. The interpretation was that of no discernible facial movement (Fig. 3A). Ten days later, upon active therapy of the subacute and chronic otitis media, a facial kinetograph showed approximately 3 mm of movement as compared to the normal of 19 mm roughly interpreted as 15 per cent return of movement (Fig. 4). Six days after this the interpretation of 65 per cent return of facial movement could be made as seen in Figure 5. Allowing for a final interpretation of 65 per cent return of function after 16 days of therapy. Utilizing several more points, including that of almost complete return, one could plot the linear relationship of return with this form of therapy on a graph against time.

TABLE I

NORMAL SMILING FACIAL KINETOGRAPHS

SUBJECT	MM MOVEMENT RT.	MM MOVEMENT LT.	MEASURED DIFFERENCE MM	% ERROR THROUGH SKEW	CORRECT DIFFERENCE MM
1. M.D.	18.50	19.50	1.00	0% *	1.00
2. C.C.	12.50	19.75	7.25	0%	7.25
	15.50	16.00	.75	3%	0.25
3. M.B.			No Movement on First Examination		
4. M.D.			No Movement on First Examination		
5. M.M.	25.00	26.00	1.00	2%	1.00
	20.00	22.00	2.00	1%	2.00
6. G.R.	21.00	23.00	2.00	0%	2.00
7. J.H.	23.00	27.50	4.50	7%	2.00
8. A.F.			No Movement on First Examination		
9. S.S.	2.25	2.50	0.25	1%	0.25
	15.00	15.00	0.00	2%	0.00
10. A.H.	22.00	18.00	4.00	0%	4.00
11. D.W.	19.50	17.50	2.00	0%	2.00
12. N.B.			Improper Exposure		
13. M.C.	21.50	21.75	0.25	3%	0.50
14. M.C.	21.50	25.75	4.25	1%	4.25
15. D.S.	21.00	20.00	1.00	3%	0.50
16. A.B.	18.00	18.00	0.00	1%	0.00
17. M.T.	22.00	23.25	1.25	1%	1.25
18. J.D.	18.50	16.00	2.50	1%	2.50
19. E.W.	8.00	9.00	1.00	1% h	1.00
20. A.H.	19.00	19.50	0.50	1% h	0.50
21.			Case Misplaced		
22. M.P.			Very Slight Movement Bilateral h		
23. M.L.	20.75	19.50	1.25	1% h	1.25
24. M.D.			No Movement		
25. M.C.	21.00	21.00	0.00	1% h	0.00
26. R.C.			Poor Exposure		
27. B.G.	14.00	17.00	3.00	3% h	3.50
28. D.G.	29.50	29.00	0.50	.5% h	0.50
29. T.G.	20.00	21.00	0.00	1% h	0.00
30. M.P.	7.20	10.50	3.30	2% h	3.30
31. A.S.	13.00	11.00	2.00	1% h	2.00
32. M.K.	10.00	7.00	3.00	6% h	1.50
33. F.F.	20.50	22.00	3.25	16% h	0.25
34. N.F.			Poor Technique		
35. E.H.	16.00	16.25	0.25	0% h	0.25

* Less than 2% error is not corrected since the fractions of mm are beyond estimation.

h - utilizing head support

COMMENT

The facial kinetograph evolved when it was clear that, despite the large number of observations made in the paper of Parks and Watkins,[2] many clinicians are dependent upon small case groups. Since one cannot always increase the size of a single group, he may be able to establish the observable differences to a point where they can be compared to similar groups in other geographical areas by other investigators at different times.

After a survey of the literature, a new therapeutic approach has been undertaken utilizing Wydase, a tissue spreading agent containing hyaluronidase which is to be presented in detail at a later date. The consideration, that an injection of a spreading agent at the stylomastoid foramen and behind the tympanic membrane, might help to determine the creditability of edema of the facial canal, arose from a conviction that more attention should be given to the possibility that a viral perineuritis is the etiology for most idiopathic facial paralysis. This, because of several observations, that seem to be drawn to one's attention more and more often with each case of acute Bell's palsy that is seen. They are:

a. A large majority of the patient's complaints are of a generalized feeling of malaise often similar to that associated with upper respiratory infections. This lasts only a day or two and is present at the outset of the acute phase of paralysis.

b. Many of the more observant patients notice that the paralysis comes on gradually over a period of several hours and these patients stand out in sharp contrast and contradistinction to those patients who simply say that they were watching television when it suddenly happened. What they often mean is, they first noted the onset of a sharp sticking pain which is often first perceptible in the occipital regions rather than sudden complete facial paralysis. This frequently is interpreted as a full feeling on that side of the head and finally is localized to a point immediately beneath the external auditory meatus which is very commonly found to be tender for the next six to eight days throughout the acute phase of the illness.

c. This point of tenderness lies directly over the facial trunk as it exists from the stylomastoid foramen and to present appearances may be clearly defined and influenced by injections of a spreading agent, as will be described in a forthcoming publication.

d. It is extremely unusual to have a bilateral idopathic paralysis of the VII nerve and, therefore, one cannot help but be drawn to

TABLE II

FACIAL KINETOGRAPH
PARALYSIS CASES

DATE	SUBJECT	HISTORY	MM MOVEMENT RT.	MM MOVEMENT LT.	MEASURED DIFF. MM	% ERROR THROUGH SKEW	CORRECTED DIFF. MM	INTERPRETATION
12/20/57	1. A.D.	Old lt. facial with clinical weakness	17.50	3.25	14.25	1%	14.25	15% of normal
1/17/58	2. A.D.	9 day postop. Lt. facial n. graft	21.25	0.00	+	2%	+	Complete left facial
12/28/57	3. E.E.	Preop slitting of facial n .Sheath	0.00	20.50	+	0%	+	Complete left facial
1/7/58	"	10 days postop	3.00	19.00	16.00	2%	16.00	Evidence of slight return
1/13/58	"	16 days postop	12.50	20.50	8.00	3%	8.75	65% return to normal
3/1/58	4. I.W.	Lt. Bell's Palsy Wydase injections	0.00	11.00	+	4%	+	Complete right facial
3/5/58	"	"	0.00	5.00	+	1%	+	Complete with slight return of passive tone
3/10/58	"	"	0.00	19.00	+	1%	+	Complete with definite return of passive tone still complete
3/19/58	"	"	0.00	24.00	+	1% h	+	still complete
3/5/58	5. A.K.	6 days postop. slitting of facial nerve sheath	10.00	15.25	5.25	1%	5.25	right 65% return to normal
3/10/58	6. V.D.	Slight rt. facial by Hx only	22.50	25.00	2.50	1%	2.50	difference is within limit of error of method
3/23/58	7. E.H.	4 months rt. paralysis in 1940, clinical weakness	15.00	22.00	7.00	1%	7.00	Approx. 65% of normal rt. function
3/24/58	8. H.B.	Lt. facial Rx Wydase 1 year ago	14.00	7.00	7.00	2%	7.00	Approx. 50% normal lt. function

+ No difference calculable due to complete paralysis on one side
h - utilizing head support

the very unique circumstances of the VII nerve, in that it passes directly through the substance of a gland which is certainly susceptible to viral infections.

e. The direct association of decreased parotid secretions of the affected side is often present and does not seem to be directly due to similar paralysis of the parasympathetic or sympathetic pathways supplying the affected parotid gland; it may more likely be the manifestation of a virus disease.

The above method is presently being utilized in patients receiving an injection of Wydase, ranging from 150 to 1,500 T. R. units in 1 cc of saline at the stylomastoid foramen and behind the tympanic membrane. One such case is indicated in this paper only by way of utilization in demonstrating the use of the facial kinetograph in paralyzed cases (Table II).

Most new methods depend upon repeated case application and statistical analyses to prove their real merit; this one is certainly far from an exception. It will be up to the clinician to weigh the merits of the information gained versus radiation involved in a single film for the knowledge in individual cases and knowledge of a group as a whole.

It is hoped that those seeing the frequent cases during their six-day acute stage do not jump to accept any therapy, before completing studies such as electromyography, salivary and serum compliment fixation tests, cytology and facial kinetography.

SUMMARY AND CONCLUSION

The facial kinetograph, a roentgenographic method for the documentation of facial nerve paralytic changes, has been described; materials, methods and techniques outlined; and the results and interpretations analyzed.

In the comment, an effort was made to establish this clinically easily adaptable method for general use to represent all facial paralysis cases in graphic form in order that small case groups may be utilized in such studies as the author has undertaken with hyaluronidase injections at the stylomastoid foramen and behind the tympanic membrane.

MASSACHUSETTS EYE AND EAR INFIRMARY

Grateful acknowledgment is made to Dr. A. S. MacMillan, Dr. A. S. McMillan, Jr. and Dr. John Irwin for their assistance.

REFERENCES

1. Martin, Hayes, and Helsper, James T.: Spontaneous Return of Function Following Surgical Section or Excision of the Seventh Cranial Nerve in the Surgery of Parotid Tumors. Ann. of Surg. 146:5:715-727 (Nov.) 1957.

2. Park, Herbert W., and Watkins, Arthur L.: Facial Paralysis—Analysis of 500 Cases. Arch. of Phys. Med. 30:749-761 (Dec.) 1949.

3. Sullivan, Joseph A.: The Surgical Treatment of Facial Palsy by an Autoplastic Nerve Graft. Can. Med. Assn. Jour. 31:474-479, 1934.

4. Sullivan, Joseph A.: A Modification of the Ballance—Duel Technique in the Treatment of Facial Paralysis. Trans. Acad. Ophthal. and Otolaryngol. 1936.

5. Sullivan, Joseph A.: Recent Advances in the Surgical Treatment of Facial Paralysis and Bell's Palsy. Laryngoscope 62:5:449-460 (May) 1952.

6. Sullivan, Joseph A., and Smith, J. Brydon: The Otological Concept of Bell's Palsy and Its Treatment. ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY 59:4:1148-1173 (Dec.) 1950.

7. Sullivan, Joseph A., and McAskile, Kenneth: Injuries to the Ear and Facial Nerve. Dis. Ear, Nose and Throat, Butterworth and Co., Ltd., 1952.

8. Tschiassny, Kurt: Eight Syndromes of Facial Paralysis and Their Significance in Locating the Lesion. ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY 62: 3:677-692 (Sept.) 1953.

9. Tschiassny, Kurt: Topognosis of Lesions of the Facial Nerve. Jour. Internat. Coll. Surg. 23:3:381-387 (Mar.) 1955.

10. Tschiassny, Kurt: A Method of Locating the Lesion in Facial Nerve Paralysis. Amer. Acad. Ophthal. and Otolaryngol., Instruction Section, 1952.

11. Collier, Josephine: Facial Paralysis. Modern Trends in Dis. Ear, Nose and Throat. Butterworth and Co., Ltd., London.

12. Harrison, K.: The Ramsay Hunt Syndrome. Proc. Royal Soc. Med. 47:5: 371-384 (May) 1954.

13. Maxwell, James H.: Repair of the Facial Nerve After Facial Lacerations. Trans. Acad. Ophthal. and Otolaryngol. (Sept.-Oct.) 1954.

14. Lathrop, Frank D.: Management of Traumatic Lesions of the Facial Nerve. A.M.A. Arch. Otolaryngol. 55:410-416 (Apr.) 1952.

15. Lathrop, Frank D.: Affections of the Facial Nerve. Bull. N. Y. Acad. Med. Second Series 28:12:796-808 (Dec.) 1952.

16. Lathrop, Frank D.: Affections of the Facial Nerve. J.A.M.A. 152:19-25 (May 2) 1953.

17. Lathrop, Frank D.: The Surgical Clinics of North America. W. B. Saunders Co., Philadelphia and London.

18. Kettel, Karsten: Facial Palsy of Otitic Origin. Arch. of Otolaryngol. 37: 303-348 (Mar.) 1943.

19. Kettel, Karsten: Neurinoma of the Facial Nerve. Arch. Otolaryngol. 44: 253-260 (Sept.) 1946.

20. Kettel, Karsten: Abnormal Course of the Facial Nerve in the Fallopian Canal. Arch. Otolaryngol. 44:406-408 (Oct.) 1946.

21. Kettel, Karsten: Melkerson's Syndrome. Arch. Otolaryngol. 46:341-360 (Sept.) 1947.

22. Kettel, Karsten: Suggestions on the Surgical Repair of Facial Palsies of Otitic Origin. Trans. Amer. Acad. Ophthal. and Otolaryngol. (July,Aug.) 1947.

23. Kettel, Karsten: Bell's Palsy. Arch. of Otolaryngol. 46:427-472 (Oct.) 1947.

24. Kettel, Karsten: The Prognosis of Nerve Grafting and Nerve Suture in Peripheral Facial Palsies. Acta Laryngologica Supplementum 84:180, Stockholm, 1948.

25. Kettel, Karsten: Peripheral Facial Paralysis in Fracture of the Temporal Bone. Arch. Otolaryngol. 51:25-41 (Jan.) 1950.

26. Kettel, Karsten: Nerve Grafting and Nerve Suture in Postoperative Facial Palsies. Danish Med. Bull. (Nov.) 1954.

27. Kettel, Karsten: Ischaemic Facial Palsy. Danish Med. Bull. (Nov.) 1954.

28. Kettel, Karsten: Decompression of the Facial Nerve in Cases of Hemifacial Spasm. Danish Med. Bull. (Mar.) 1955.

29. Taylor, Craig L., and Blaschke, Alfred C.: A Method of Kinematic Analysis of Motions of the Shoulder, Arm and Hand Complex. Ann. N. Y. Acad. Sci. 51: Article7:1251-1265.

30. Redding, Foster, and Gammon, George D.: A New Device for Recording Motion in Three Dimensions with Illustrative Application to the Study of Tremor. Trans. Amer. Neurolog. Assn. pp. 210-211, 1954.

PERTINENT PAPERS FOUND ON A REVIEW OF THE LITERATURE WHICH WERE NOT PRESENTLY AVAILABLE

1. Melgar, Pacchiano L.: Revista De Savided Melitar—Mexico, 10(1-6) pp. 44-52 (Jan.-Mar.) 1957.

2. Rathmell, T. K.: Seminar Philadelphia, 17(3) Fall-Winter 1955.

3. Shapenshtein, D. J., and Iordanskaia, E. M.: Fizologicheskii Zhurnal S. S. R. Imeni I. M. Scehenova (Moskow) 41(1):35 (Jan.-Feb.) 1955.

4. Hall, J.: Med. and Biol. Illustration (London) 4(4):213-222 (Oct.) 1954.

5. Taylor, C. L., and Blaschke, A. C.: Schweiz Med. Wchnschi 80:25:1260-1261 (Nov.) 1950.

6. Straus, E. W.: Amer. Jour. Psychiatry 108:439 (Dec.) 1951.

7. Miilli, A.: Resenha Clin. Client. 17:299-302 (Aug.) 1948.

8. Balli, R.: Jour. of Abnormal and Social Psychology 38:250 (Apr.) 1943.

XIX

LYMPHOSARCOMA: A PROBLEM FOR THE NOSE AND THROAT SPECIALIST

ALBERT P. SELTZER, M.D.

PHILADELPHIA, PA.

Lymphosarcoma of the upper respiratory tract is a malignant growth that is said to be comparatively rare at all ages, especially in the young. Instances have been reported in very early childhood, as well as the sixth decade or later. Thus, this rarity is of considerable interest, since the abundance of lymphoid tissue in this region, partly represented by Waldeyer's ring, would seem to favor its occurrence there.

Lymphosarcoma, in Mallory's opinion, is only one manifestation of a disease condition which may also occur in other forms, a lymphocytoma, lymphoma, lympholeukemia, Hodgkin's disease, and others of a similar nature.

By lymphoid is understood a tissue made up of masses of usually small round mononuclear cells in a supporting fibrous reticulum, familiarly seen in lymph nodes, and in some mucous membranes as in the intestinal canal (Peyer's patches).

The cells called lymphocytes appear in the stained specimen as a nucleus, which stains a deep blue, surrounded by a narrow layer of pale blue cytoplasm. They form the larger part of lymphoid tissue, and are also present in the circulating blood as a mononuclear form of leucocyte with some variation in their size and in the relative proportion of nucleus to cytoplasm.

Lymphosarcoma is considered to be the most important malignant growth of lymph nodes. It has been observed to occur twice as frequently in males as in females, and at any age, as has been noted, but more often in the fifth and sixth decades. It develops comparatively slowly, with more rapid later growth and with exceedingly rare recovery with any treatment.

From the Department of Otolaryngology, Albert Einstein Medical Center, Southern Div., Philadelphia.

It begins most often with the enlargement of a group of lymph nodes, or rarely of a single node, and grows to penetrate the capsule, extending into the surrounding tissues, with in some cases further extension by metastasis to more distant regions.

Microscopically, the tumor tissue is richly supplied with blood vessels; mitoses are present, and there may be hemorrhagic areas, and sometimes ulcerations.

Clinically, one diagnostic sign of tonsillar lymphosarcoma is the notable enlargement of only one tonsil; the surface may be rounded and smooth, or it may be nodular sometimes to a degree that has been called polypoid. The tumor is usually soft, and may bleed easily, even if brushed with a cotton applicator, or there may be ulceration of the surface.

Accepted treatment of lymphosarcoma of the tonsil includes, first of all, radical excision of the involved tissue. If the growth is still sharply localized, there is a possibility of complete removal and recovery. But as in other cases of malignant growths, the patient is seldom seen early enough to accomplish this end, in which case, treatment can be only palliative, with irradiation following the removal of the malignant focus.

The general effect of the radiation treatment will depend on the rapidity of the tumor growth. Some have been described as more or less chronic. In cases where there is rapid growth, although the irradiation may be followed by apparent arrest, this effect is usually only temporary and is soon followed by re-appearance of the tumor, with later metastasis to distant parts of the body. The following case seen by the writer presents points of interest:

REPORT OF A CASE

Male, Negro, 31 years of age. The patient complained of sore throat, mainly on the right side. He said that his tonsils had been removed five weeks earlier, though the history at the hospital where this was done recorded a tonsillectomy at the age of seven years. He complained also of difficulty in speaking and swallowing; that the latter had interfered with his taking food, with a consequent considerable loss of weight. The earlier history mentions tube feeding. A throat examination showed a growth about the size of a large bean in the tonsillar fossa on the right side. On palpation, it appeared to be about the same consistency as that of the surrounding tissues. He

asked that the growth be removed, and on March 22, 1957, he was admitted to the writer's service at the hospital, where a complete physical examination was reported negative in all fields, except the right side of the pharynx, as noted above, where there was a mass in the right tonsillar region, and cervical adenopathy. A biopsy on this tumor tissue gave a report of lymphosarcoma. Since the earlier throat operation, the patient had been receiving irradiation treatment to the right side of the neck, with definite diminution of the enlarged cervical nodes.

At the time of the present operation, the patient asked that he be given general anesthesia, as the previous one, which had been done with a local anesthetic, was too painful. Accordingly, he was given intravenous sodium penitothal with general anesthesia. The tab of tonsillar tissue was grasped with a snare, and the growth was removed. The procedure took only a few moments, but the resulting bleeding was finally controlled only after about an hour and a half.

On recovery from this operation, the patient was discharged, but was re-admitted and discharged from the hospital four times between March 22, 1957 and July 17, 1957 during which time the treatment, other than surgical or x-ray, consisted of the administration of cortisone, ACTH, and nitrogen mustard.

While in the hospital in July, 1957, the patient began to have difficulty in breathing, and a tracheotomy was done following an endoscopy. The report on this examination revealed a "firm ulcerating mass, covered with necrotic tissue, involving the right side of the hypopharynx and the base of the tongue"; there was also edema of the glottis, but a note mentions that "the airway is adequate." Neither the floor of the mouth, nor the left side of the throat were involved at that time.

By August 5, 1957, there was definite shortness of breath, and an unsuccessful attempt was made to secure an adequate airway by the insertion of a bronchoscope. This attempt having failed, the larynx was exposed by means of an adolescent laryngoscope, which showed the epiglottis and nearbly areas were extensively involved. This procedure led to complete respiratory obstruction, and cyanosis developed. To relieve this condition, a tracheotomy was done at once by making a vertical incision of the skin at the lower border of the thyroid cartilage, extending about one inch downward, and introducing a No. 6 tracheotomy tube to provide an airway. For a short time, artificial respiration was carried out, with the administration

of oxygen through the tracheotomy tube, to which the patient responded promptly. The wound was packed with plain ribbon gauze, and a dressing applied. By the time the patient left the operating room, a good airway had been established.

The patient died suddenly in the afternoon of August 29, 1957, five weeks after the last admission. The recorded cause of death was "respiratory obstruction due to lymphosarcoma of the pharynx."

SUMMARY

A young colored man, whose tonsils had been removed when he was seven years old, began to have recurrent, then persistent sore throat at 31 years of age. At the time, tumor tissue was found on the throat examination, in the right tonsillar region, which was removed by surgical operation. Five weeks later, he consulted the writer for sore throat, with difficulty in swallowing and speaking, which proved on examination to be caused by a recurrent growth in the right tonsillar fossa. Biopsy of this tumor tissue confirmed an earlier diagnosis of lymphosarcoma, and a radical operation was done for the complete removal. After repeated recurrence and extension to the right cervical lymph nodes, irradiation to the right side of the neck was given, with temporary good recession of the lymph node involvement. X-ray treatment was discontinued temporarily, both because of this result on the cervical condition and also because a radiation dermatitis had developed. Medical treatment was given in the form of cortisone, ACTH, and nitrogen mustard, without favorable effect, and the pharyngeal malignancy continued to extend, to include the epiglottis and the surrounding tissues, with final respiratory obstruction, necessitating tracheotomy which gave only temporary relief, with death of the patient, seven months after the first operation for tumor.

2104 SPRUCE ST.

BIBLIOGRAPHY

1. Bremer, J. L.: Textbook of Histology. Philadelphia, Blakiston, 1944.

2. Edwards, T. M., and Baker, Jr., C. F.: Lymphosarcoma of the Tonsil. Jour. Florida Med. Assn. 42:478, 1955.

3. Fulton, J. F.: Textbook of Physiology. 17th ed., Philadelphia, Saunder, 1955.

4. Hirst, O. C., and Charland, R. A.: Lymphosarcoma of the Tonsil. Arch. Otolaryngology 54:60, 1951.

5. Karsner, H. T.: Human Pathology. 7th ed., Philadelphia, Lippincott, 1949.

6. Levenson, S. A., and McFate, R. P.: Clinical Laboratory Diagnosis. 5th ed., Philadelphia, Lea and Febiger, 1956.

7. MacCallum, W. G.: Textbook of Pathology. 7th ed., Philadelphia, Saunder, 1940.

8. Metson, B. F.: Lymphosarcoma of the Tonsil in Children. ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY 63:193 (Mar.) 1954.

9. Rainey, J. J.: Lymphosarcoma of the Tonsil, A Long Survival. Arch. Otolaryngol. 63:609 (June) 1956.

XX

AN ANALYSIS OF ONE THOUSAND CASES OF HEARING LOSS IN CHILDREN

FRANK KODMAN JR., PH.D.

GERALD SPERRAZZO, M.A.

LEXINGTON, KY.

A sample of 95,000 school children was tested with individual and group methods of pure tone audiometry. The details of this study will be found in an as yet unpublished manuscript by Kodman[12] who served as technical director of the testing phase of the project. The present study concerns an analysis of 1,000 children with hearing loss who were selected at random from the hearing loss group. Hearing loss was defined as two or more thresholds of 25 db or greater at the octave frequencies of 250, 500, 1,000, 2,000, 4,000 and 8,000 cycles in either ear.

Of special interest are the mean thresholds of the group for the test frequencies 250, 500 ,1,000, 2,000, 4,000 and 8,000 cycles. Figure 1 is a plot of the thresholds. The results show a flat loss with the exception of the threshold at 4,000 cycles. Chi square was computed and found to be 1.176 which is not significant for five degrees of freedom. We cannot, therefore, reject the null hypothesis of the differences between the thresholds being attributable to chance.

In Figure 2 the mean thresholds are plotted for the right and left ears of the females; in Figure 3, of the males. In both Figures 2 and 3 the left ears show the greater loss. These differences will be subjected to statistical test. The reader will note the parallel difference between the ears of both sexes.

LOSSES BETWEEN RIGHT AND LEFT EARS

The following hypotheses are offered in the analysis of these cases.

1. There will be a significant difference between the number of losses in the right ear in males and females.

TABLE I

	MALES	FEMALES	X^2	SIGNIFICANT
Rt. ear	333	338	.036	No
Lt. ear	398	397		No
Both ears	731	737		No

2. There will be a significant difference between the number of losses in the left ear in males and females.

3. There will be a significant difference between the number of losses in both ears.

In Table I are shown the results of the chi square (X^2) test of significance applied to the data to evaluate the three hypotheses above.

The results of the chi squares do not support the hypotheses. In other words, there was no statistical difference between the right ears of males and females or between the left ears of males and females or between both ears of males and females.

LOSSES BETWEEN EARS WITHIN SEX

To evaluate the ears within sexes, the following hypotheses are offered.

1. There will be a significant difference in the number of losses among the right ears of the males.

2. There will be a significant difference in the number of losses between the right and left ears of the females.

3. There will be a significant difference between the right and left ears of both sexes.

In Table II are shown the results of the chi square analysis applied to the data to evaluate the above hypotheses.

TABLE II

	RT. EAR LOSSES	LT. EAR LOSSES	X^2	P
Males	333	398	5.76	.05
Females	338	399	5.03	.05
Total	671	797	10.94	.01

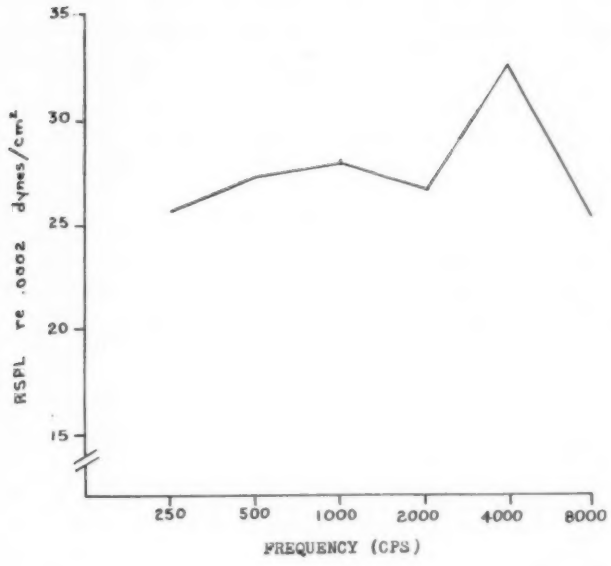


Fig. 1.—Group audiogram for the hearing loss group. Mean thresholds at each test frequency. N = 2000.

In the right hand column, the reader will note that the differences between the right and left ears for each sex is significant at the .05 level. The differences between the right and left ears of both sexes is significant at the .01 level. Thus we can conclude that there was a significantly greater number of hearing losses in the left ears of both the males and the females.

MONAURAL LOSSES

There were 102 right ear monaural losses and 129 left ear monaural losses in the male hearing loss group. A chi square of 3.155 was not significant. For the females there were 66 right ear monaural losses and 131 left ear monaural losses. A chi square of 21.446 is statistically significant at the .01 level. This means that there were more monaural losses in the left ears of the females in the hearing loss group than could be expected on a chance basis.

Examining the number of monaural losses between sexes, a significant difference was found between the right ears. There were 102 right ear monaural losses in the males and 66 right ear monaural losses in the females. A chi square of 7.714 is significant at the .01 level. Thus we can conclude that monaural loss occurred with greater frequency in the right ears of the males than in the right ears of the females. No difference was found for the left ears.

BINAURAL LOSSES

There were 269 binaural losses in males and 277 in females. A chi square of .117 is not significant. In Table III is shown the incidence of monaural versus binaural losses between sexes.

TABLE III

	NUMBER OF MONAURAL LOSSES	NUMBER OF BINAURAL LOSSES	X^2	P
Males	231	269	2.888	
Females	197	277	13.50	.01
	428	546	14.295	.01

The results show a significant difference between the number of binaural losses versus monaural losses for the females. The females had a greater number of monaural losses in the left ear than in the right ear. This was not found for the males. The females also showed a greater number of binaural than monaural losses. For the total sample, binaural losses also occurred significantly oftener than monaural losses.

Previous investigators have noted the possibility of differences in the incidence of hearing loss among ears within and between sexes. In the present investigation, no statistical difference was found between the number of losses for the right ears of the males and females or between the number of losses for the left ears.

Significant differences were found in the incidence of losses between ears within sexes; in other words, there was a significantly greater number of losses in the left ears of both males and females. Why there should be more losses in the left ear than in the right ear of each sex is not readily explained.

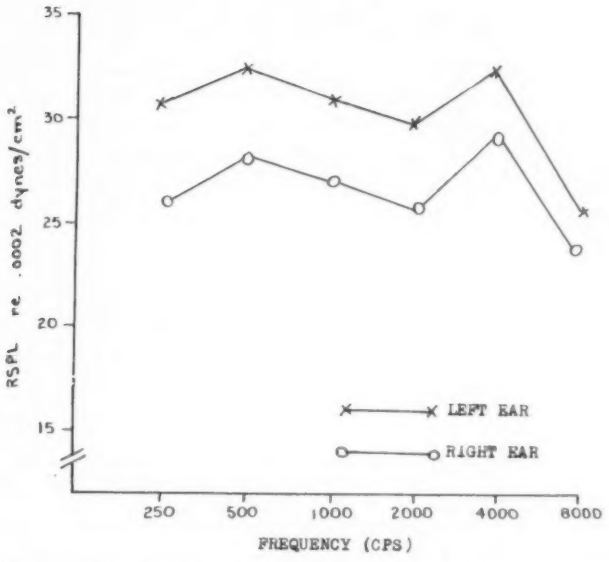


Fig. 2.—Mean thresholds for the right and left ears of the female group.

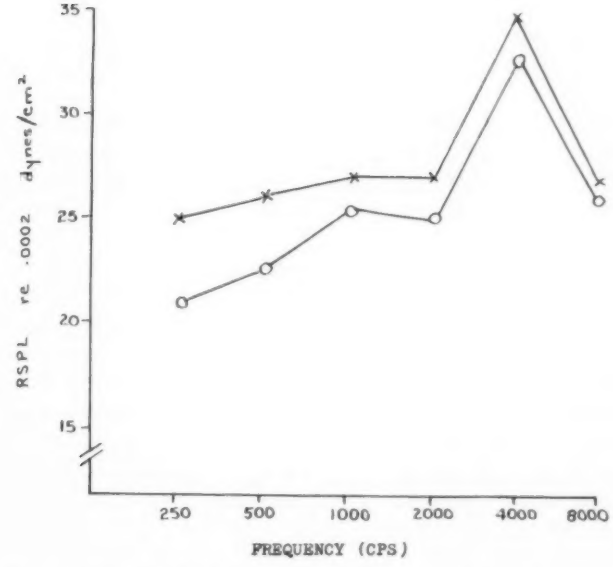


Fig. 3.—Mean thresholds for the right and left ears of the male group.

COMPARISON OF FINDINGS WITH OTHER STUDIES

There is a consensus of opinion that approximately five per cent of public school children in the United States have a hearing loss that warrants medical or educational attention or both. In the present survey, approximately five per cent of the children had a mild-to-severe hearing loss. In 1950 the Scottish Education Department, Edinburgh, reported their incidence of hearing loss as ranging from five to eight per cent for school children.[14]

Curry,[1,2] Goldman[8] and Kodman, Acuff and Stockdell[9] did not find a statistical difference between monaural and binaural hearing losses. This was not supported by the present study which found that binaural losses occurred significantly oftener than monaural losses.

Previous investigators, Curry,[1,2] Goldman,[8] Glorig, et al.,[7] and Steinberg, Montgomery and Gardner[13] found that males had a significantly greater number of hearing losses than females. There was a tendency toward a greater number of losses in the males in the present sample; however, the trend was not statistically significant. The incidence of loss for the males was 5.26 per cent and for the females 4.74 per cent.

Losses occurred more frequently in the left ear in both sexes. Glorig et al.[7] tested a sample of 3,500 persons ranging in age from 10 to 79 years and also found significantly more left ear losses than right ear losses in each sex. They did not find that handedness and the better ear were significantly related. There was also no statistical difference between the numbers of right handed and left handed persons who had better hearing in the left ear.

Consideration has been given to the classroom teacher's ability to detect mild-to-severe hearing losses in pupils. Curry,[3,4] Geyer and Yankauer[6] and Kodman[10] have found that the teacher did slightly better than chance in detecting hearing loss pupils. Kodman et al.[11] evaluated teachers and parents in their ability to detect hearing loss in pupils. In both cases, pure tone audiometry was far superior in detecting hearing losses. The major conclusion to be drawn is that public school audiometry is needed to safeguard the auditory sensitivity of our school children and thus insure them equivalent educational opportunity.

UNIVERSITY OF KENTUCKY

REFERENCES

1. Curry, E. T.: Analysis of Hearing Loss Patterns in a Rural Illinois School System. Amer. Jour. of Diseases of Children 80:254-259, 1950.

2. Curry, E. T.: An Analysis of Hearing Loss Patterns in a Rural Illinois School System. Eye, Ear, Nose and Throat Monthly 29:357-359, 1950.

3. Curry, E. T.: The Efficiency of Teacher Referrals in a School Hearing Testing Program. Jour. of Speech and Hearing Disorders 15:211-214, 1950.

4. Curry, E. T.: Are Teachers Good Judges of Their Pupils' Hearing? Jour. of Exceptional Children 21:15-17,19, 1954.

5. Edwards, A. L.: Experimental Design in Psychological Research. Rinehart Co., New York, 1950.

6. Geyer, M. L., and Yankauer, A.: Teacher Judgment of Hearing Loss in Children. Jour. of Speech and Hearing Disorders 21:482-486, 1957.

7. Glorig, A., et al.: The 1954 Wisconsin State Fair Hearing Survey. Amer. Acad. Ophthal. & Otolaryngol. 1-111, 1957

8. Goldman, S.: An Investigation of Auditory Sensitivity in Elementary School Children. M.A. Thesis, University of Kentucky, 1955.

9. Kodman, F., Acuff, C. E., and Stockdell, K. G.: The Incidence of Hearing Loss in Kentucky School Children. Jour. of School Health 27:253-258, 1957.

10. Kodman, F.: Identification of Hearing Loss by the Classroom Teacher. Laryngoscope 66:1346-1349, 1956.

11. Kodman, F., Schneck, P. E., Stockdell, K. G., Thompson, B. S., and Spies, C. C.: Identification of Hearing Loss by Parents, Teachers and Audiometers. Eye, Ear, Nose and Throat Monthly 37:103-105, 1958.

12. Kodman, F.: The WHAS Crusade for Children Hearing Project, Louisville, Kentucky, 1955-1957 (Unpublished manuscript).

13. Steinberg, J. C., Montgomery, H. C., and Gardner, M. D.: Results of the World's Fair Hearing Tests. Jour. of Acous. Soc. of Amer. 12:291-301, 1940.

14. Scottish Education Department Pamphlet: Pupils Who Are Defective in Hearing. Edinburgh, Scotland, pp. 1-71, 1950.

Abstracts of Current Articles

EAR

The Significance of the Cuticular Strip for the Development of Cholesteatoma of the Middle Ear

Link, R.: Acta Otolaryng. (Stockh.) 49:411-420, 1958 (in German).

There is a difference in opinion as to the genesis of cholesteatosis. Whereas in the Anglo-Saxon literature it is generally maintained that cholesteatosis is most likely caused by metaplasia of the mucosa of the middle ear, writers from the German-speaking countries as a group have always adhered to the theory that epithelium from the external ear canal invades the middle ear spaces, mainly the attic. Opinion is divided, however, as to the primary cause of this invasion: is it a necrotizing osteitis within the middle ear, which the epithelium attempts to cover, or is it a specific "growth potential" of the epithelium itself? [The entire problem has recently been reviewed by L. Rüedi; cf. this Journal 66:283, 1957, Rev.]

The paper to be reviewed here deals with one particular aspect of the cholesteatosis problem, namely, the postulated growth potential of the epithelium of the external ear canal. The author first makes the point that the epidermis of the osseous portion of the canal is not thin and atrophic (as it is usually described) along its entire circumference, but that a well-developed strip of cutis exists along the upper wall. This latter part of the wall is made up by the squamous portion of the temporal bone, in contrast to the remainder which is formed by the tympanic portion. The vascular supply of the epithelial lining also differs within the two portions: that of the tympanic portion comes from the deep auricular, the same artery which supplies the hypotympanum, whereas the cuticular strip receives its supply from branches of the temporal and retroauricular arteries. The same vessels continue along the handle of the malleus toward the umbo to form the inner radial plexus of the ear drum and among other areas to supply Shrapnell's membrane.

Among 79 specimens dissected from human ear canals, the cuticular strip was found strongly developed in 28 cases and all these were associated with poor pneumatization of the mastoid. In contrast, well-pneumatized mastoids were invariably found to possess a thin cuticular strip of lesser development. The author reasons that the

growth of the mastoid and of the zygomatic process, both of which contribute to the formation of the roof of the external canal during the process of pneumatization, determines the development of the cuticular strip: the poorer the pneumatization, the more the cuticular strip keeps growing thus developing a strong vascular system.

In order to test the concept of the epithelial growth potential, the author conducted experiments in guinea pigs. Following the technique of Berberich, Hoshiya, a.o., artificial cholesteatomas were produced by application of cancerogenous material (.3 per cent 3-4 Benzypren in Benzol). This solution was applied daily for 16 weeks to a marginal perforation which had been surgically made for this purpose.

In twelve of the animals (group I), a transverse section of the cuticular strip was resected at the time the perforation was made so as to interfere with its blood supply. In a second group (II) of animals, the cuticular strip was left intact. All animals in group II developed histologically verified cholesteatomas within the period of observation. Of group I, seven animals did not show any signs of cholesteatoma, whereas in the remaining five the "squamous epithelium produced cyst-like or solid processes which had grown into the submucosa via the defect within the ear drum." The author believes that in the latter cases of group I the resection of the cuticular strip had not been executed with sufficient thoroughness so as to really impair its blood supply. Statistically, the difference between both groups proved to be significant.

The author concludes that the growth potential of the epidermis of the external canal is a reality and that it is a specific property of the cuticular plate which borders on Shrapnell's membrane, i.e., the area of the ear drum where marginal perforations are known to develop.

TONNDORF

Subjective Vestibular Symptomatology in Otosclerosis Patients Before and After Fenestration

Felisati, D.: Archivio Ital. Di Otologia Rinologia e Laringologia 69:26-51 (Feb.) 1958.

In a group of 87 otosclerosis patients the author studied the subjective vestibular symptomatology before fenestration surgery, immediately after surgery, and within the next four years. The cases have been divided into three groups. Group A consists of those patients

with air conduction between 35 and 40 db for the middle frequencies (512 to 2-48) and bone conduction almost normal; group B, air conduction between 40 and 60 db and bone conduction corrected following Carhart, with a loss of more than 10 db in one of the middle frequencies; group C air conduction between 60 and 80 db and for the corrected bone conduction a loss of more than 10 db for two or three of the middle frequencies. Sixty-seven patients were operated upon using the Lempert technique and 20 using the Wullstein technique. The vestibular symptoms are divided into three groups: one, slight disturbances of balance or light-headedness; two, spontaneous dizziness aggravated by movements of the head and disturbance of balance; three, marked dizziness with disturbances of balance and neurovegetative symptoms of marked degree. Subjective vestibular disturbances were observed in 30 per cent of patients; of 26 subjects 22 were women and 4 were men. The vestibular symptoms were never so severe as to cause real ménièriform crises.

Vestibular symptoms occur more frequently in A and B cases. However with progression of the otosclerotic disease as seen in C cases there is an aggravation of symptoms which the author attributes to alterations of the circulation which affect the hydrodynamics of the labyrinth, or possibly stimulation of the neuroepithelium, when the otosclerotic lesion invades the labyrinth. Tinnitus appeared before the hearing loss in 80 per cent of the patients.

In the first week after fenestration there was a symptomatology of the third degree in 69 per cent of the patients; in 22 per cent there was a symptomatology of the first and second degrees; 9 per cent had no symptoms. The author believes that within the first 30 days complete labyrinthine balance is seldom obtained. After three months there were no patients with severe vestibular disturbances and only in 55 per cent were there symptoms of the first and second degree. After one year only 15 per cent had a symptomatology of the second degree and 23 per cent a symptomatology of the first degree. After four years 28 per cent had symptoms of the first degree. Women were more commonly affected than men. Patients operated upon by the Wullstein technique were less disturbed than those operated upon by the Lempert technique. The author believes there are two reasons for this: first, in the Wullstein technique the fenestra is opened in the canal instead of near the ampulla as in the Lempert technique; second, a different kind of flap is used to cover the window. The author stresses the fact that the best results usually occur among the patients who develop the least signs of postoperative labyrinthitis.

DE GASPARI

Menière's Syndrome

Nakamura, S., et al: Otolaryngology (Tokyo) 31:1-9 (Jan.) 1959.

Audiologic investigation of forty cases in which the clinical syndrome was suggestive of Ménière's disease is recorded.

The authors divided the cases into five groups:

a. Tinnitus with impaired hearing without dizziness 5

b. Tinnitus and impairment of hearing preceding dizziness 4

c. Hearing impairment and dizziness with simultaneous onset 7

d. Dizziness preceding tinnitus and hearing loss 12

e. Dizziness without hearing loss and tinnitus 12

The authors investigated their cases on the basis of pathological changes due to 1) labyrinthine hydrops, 2) labyrinthine ischemia, and 3) labyrinthine apoplexy. In only one instance was an allergic history obtained.

They believe from their study that loss of low tones appeared in the initial stage of the disease, and that it was reversible. But when the condition lasted several weeks and months the impairment of hearing progressively involved the higher tones and was irreversible. Tinnitus in the earlier stage of the disease was usually low tone and as this symptom persisted the higher range became involved. There were 11 patients with caloric reactions below normal and 21 were thought to be within normal limits. There were no cases in which the caloric reaction was exaggerated.

To differentiate the labyrinthine changes, the importance of the role of recruitment and auditory threshold fatigue tests were presented. The authors believe, in the light of their study, the term Ménière's disease should be replaced by the more descriptive name of labyrinthine hydrops.

HARA

Medical Treatment of Ménière's Disease

Yamasaki, Y.: Otolaryngology, Tokyo, 31:10-12 (Jan.) 1959.

Since Ménière's publication on the disease bearing his name in 1861, numerous workers in this field have attempted to clarify the

basic cause of its etiology. No definite theory has been universally accepted. Thus the therapy has been aimed at correction of, among other things, water metabolism, allergic factor, nutritional imbalance, disturbance of the autonomic nervous system, vascular and hormone deficiencies.

During the past five years, 48 patients with Ménière's syndrome were treated in the ear, nose and throat department of Niigata University. Drugs were selected 1) to influence the autonomic nervous system, 2) the vascular supplies, and 3) for control of histamine. Dizziness was relieved in 61 per cent of the cases, tinnitus in 41 per cent, and impairment of hearing in 25 per cent. The author feels that the best drugs were those which act on the blood vessels through the autonomic nervous system. Among these are 1 per cent procaine hydrochloride, priscoline hydrochloride and chlorpromazine. To stimulate vascular dilatation nicotinic acid, hypertonic sodium bicarbonate were tried but the results were indifferent. To control histamine, dramamine, travelmine, and histamine I.V. were tried. Chances of cure appear to be greatest when treatment is instituted early in the disease and well nigh hopeless when the condition reaches the chronic stage.

HARA

Results of Tympanoplasty in Various Age Groups

Bocca, E.: Archivio Ital. Otologia Rinologia e Laringologia 69:1-7 (Feb.) 1958.

The author reports the results of 212 tympanoplasties which were controlled postoperatively for at least three months. The patients are divided into four age groups: group I, patients 15 or younger; group II, from 15 to 25; group III, from 25 to 50; group IV, over 50 years of age. The author's study indicates that the overall results of all types of tympanoplasty are better in patients of the first two groups (age 25 or younger) than in groups III or IV (over the age of 25). An analysis of results of the various types of tympanoplasty reveals that in the group of patients which had type I tympanoplasty (ossicular chain intact), the hearing improvement is more uniform than in the other two types of operations. (Type II: the stapes is present, type III: stapes missing). Much better results are obtained in type I and II tympanoplasty in patients below the age of 15.

DEGASPARI

Observations on the Sense of Hearing in the Blind

Niccoli Vallesi, R., and *Salis, B.*: Bolletino Delle Malattie Dell'Orechio, Della Gola, Del Naso, Vol. 76 (July-Aug.) 1958.

The authors point out that it has been established that in the blind there is no evidence of any sharpening of the other senses, such as hearing. Their study is an analysis of the acuity of hearing in 140 blind persons between the ages of 15 and 45. Three audiometric tests were performed in each case: pure tone, speech reception, and discrimination.

A psychometric evaluation was also done in order to determine each person's sense of orientation, rapidity of intuition, and reaction time. One hundred controls were tested in like manner. Many cases of deafness were found among the blind. The most common type was a mixed deafness. An interesting finding was that among 20 of the blind who had nerve deafness, seven also had retinitis pigmentosa. The authors conclude that contrary to former beliefs there is impairment of hearing in many blind persons. They do not exclude the possibility that in some of them perceptive acuity above normal can be found.

DEGASPARI

Prediction of Ossicular Pathology in Chronic Suppurative Otitis Media

Rebagliatti, Hector: Anales de Oto-rino-laringologia del Uruguay 28:Part II:83, 1958.

The author stresses the need for conservatism in temporal bone surgery. In addition to the findings in otoscopy and by means of x-rays, the surgeon should attempt to diagnose with a high degree of accuracy the status of the ossicular chain; in this way he can plan his surgical attack and tailor his technique more accurately to each individual case. Two tests are employed for this phase of the examination: 1) the acoustic probe and 2) the cotton prosthesis. This study is limited to the author's experience with the cotton prosthesis as a diagnostic tool. When the closure of a perforation or the blockage of either the oval or round window (with the cotton prosthesis) results in improved hearing, it must be assumed that the ossicular chain is functioning normally. If no improvement in threshold can be obtained, interruption of the chain must be suspected. The author quotes Zanotti who reported 150 cases in which cotton prosthesis was

used to predict the pathology of the ossicles and later compared these findings with those at the time of the operation. The cases were divided into three groups.

Group I. Pure tone loss of 30 db or less. Most of these had a positive cotton prosthesis test and the only lesions found at time of surgery was the perforation of the tympanic membrane. In the few cases which had a negative response in the cotton prosthesis test surgery revealed various lesions of the ossicular chain but intact oval and round windows.

Group II. Cases with a threshold for pure tones of 35 to 50 db. Although two-thirds of the cases in this group had positive prosthesis tests it was found at the time of surgery that all of them had some abnormality of the ossicles. Both windows were normal. Zanotti attributes the improved hearing with the cotton prosthesis to granulation tissue and small adhesions which bridge over the interrupted ossicular chain.

Group III. The cases in this group had a hearing loss of 50 db or more. In most of these cases the ossicles were partially or totally destroyed and the cotton prosthesis failed to improve hearing. However, in a few in which the test was positive it was noted that the oval and round windows were healthy.

The author agrees with Zanotti's conclusion that the preoperative findings with cotton prosthesis are a valuable diagnostic tool in determining the integrity of the ossicular chain and windows. He then describes the surgical technique (of Wullstein) which he employs for the various types of lesions, from myringoplasty in the group I cases to tympanoplasty and fenestration when there is suppuration and fixation of the footplate of the stapes.

ALFARO

Repair of Tympanic Perforations

Mitchell, J. F. O.: Jour. of Laryngol. and Otol. 72:9:720-29, 1958.

The author describes a modification of the cautery technique for closure of perforations. The margin of the perforation is carefully touched with a tightly wound applicator dipped in 50% trichloracetic acid taking care to avoid touching the median wall of the

middle ear. In most cases no topical anesthesia was used. With full aseptic technique a small square of gelatin sponge is soaked in the patient's own blood (1 cc obtained by venipuncture). The gelatin is placed over the perforation under direct vision, pressing it down firmly over the whitened edges. A small wool plug is inserted in the meatus and the patient instructed not to blow his nose for 48 hours. The patch clots adherent to the margins of the perforation and remains there until the defect heals after which the patch gradually migrates to the posterior wall. If the first attempt does not succeed, yet the perforation and middle ear remain clean and dry, the margin should be cauterized again on two or three occasions and then the patch procedure repeated. Of 50 perforations treated with this technique, 36 healed well; 8 persisted requiring further treatment, and 6 patients failed to report after the first treatment. Of the 36 successful cases, 14 healed after one treatment, 6 after two treatments and 16 after repeated treatments (average, 4.25 times).

ALFARO

The Exhaustion of Phono-receptors Following Exposure to Sound

Vosteen, K. H.: Arch. Ohren- usw Heilk. 172:489-512, 1958.

In the previous papers, the author had reported on enzyme studies in the cochlea. He had given evidence to the presence within the cochlear duct of "Atmungs Fermente" (in the sense of O. Warburg) at the cytological level: 1) Succinodehydrase; 2) Cytochromoxydase; 3) DPN-Diaphorase and TPN-Diaphorase. The present study is concerned with the investigation of the activity of such enzymes following sound exposure. Guinea pigs were exposed to sound pressures of 70 to 85 db at 2000 cps of various duration: brief tone 'pips' were employed as well as prolonged exposures, ranging from as brief as two hours to as long as five days.

The author was able to demonstrate a decrease of enzyme activity (succinodehydrase, which is normally concentrated at the base of each individual haircell) following prolonged exposure of several days. The cytochemical changes were apparent well before any signs of damage to the haircells could be demonstrated histologically. To be sure, signs of cellular damage were always found associated with cytochemical changes in the same specimen. The latter was predominant in the regions marginal to the center of the section of the organ of Corti receiving maximal stimulation. At the center of this area, structural damage was more pronounced, the transition

between both phenomena being a gradual one. The changes were confined to the outer haircells. After recovery periods of several weeks, neither resumption of normal enzyme activity had occurred nor has autolysis taken place of histologically undamaged cells which had previously shown decreased enzyme activity. The latter conclusion of course is based upon comparison of two different series of animals. Only when brief tone 'pips' interrupted by long silent intervals had been employed, was the magnitude of the cyto-chemical change reduced.

The author comes to the conclusion that the precipitate of an "acoustic trauma" is less a true mechanical-structural damage of the organ of Corti, but rather the end product of a complete exhaustion of the cellular metabolism of the "phono-receptors," i.e., of the haircells. (Perhaps this is a function of the magnitude of exposure: high-level exposure may result predominantly in structural damage whereas in lower-level exposure the cytochemical changes may dominate.—Reviewer.) The author concludes his report by discussing his findings in view of the presently accepted concepts of general neurophysiological metabolism.

TONNDORF

Modification of Cochlear Potentials Produced by Streptomycin Poisoning and by Extensive Venous Obstruction

Davis, H., Deatherage, B. H., Rosenblut, B., Fernandez, C., Kimura, R., and *Smith, C. A.*: Laryngoscope 68:596-627 (Mar.) 1958.

This study is a most important advance in the understanding of the biophysics of hearing.

Four electrical phenomena, the DC endocochlear potential, cochlear microphonic, summating potential and action potential are considered indices of the functional state of the cochlea. The exact sites of generation of these potentials had not previously been established. The present experiments were planned in the hope of obtaining definitive information as to the contribution made by the hair cells and the stria vascularis to these electrical responses.

It is known that streptomycin will injure the hair cells of the organ of Corti and it was recently demonstrated that obstruction of the cochlear vein will selectively cause degeneration of the stria vascularis. Therefore, streptomycin was injected into the bullae of

26 guinea pigs producing degeneration first of the external and then internal hair cells. The stria vascularis showed little change. The cochlear vein and its collaterals were obstructed in ten guinea pigs and degenerative changes were produced in the stria vascularis.

After planned time intervals to allow for some degeneration, the electrical responses were measured, the animals were sacrified and the histopathological changes in the inner ear were correlated with the electrical measurements.

The site of generation of the DC endocochlear potential had been tentatively located both in the hair cells and in the stria vascularis. These experiments offer conclusive evidence that these potentials are generated by the stria vascularis and not by the hair cells.

The cochlear microphonic was said to depend upon the hair cells. The evidence obtained strongly supports the hypothesis that the external hair cells are the site of generation of the cochlear microphonic and that the internal hair cells contribute very little.

The negative summating potential was thought to originate in the external and internal hair cells but the evidence points to the internal hair cells as the source of this potential. A small amount may come from the external hair cells. The source and significance of the positive summating potential was not established.

Action potential is generated by the nerve fibers in the modiolus and is believed to reflect the integrity of the over-all mechanical and neural systems including tectorial membrane, hair cells, nerve endings and nerve fibers.

SENTURIA

Vestibular Syndrome Followed by Epidemic Parotitis

Rinaldi, L.: Bolletino Delle Malattie Dell'Orechio, Della Gola, Del Naso 76:388-396 (July-Aug.) 1958.

The author reports the case of a 42 year old woman who suffered a vestibular crisis on the right side, and 20 days later developed mumps. The cochlear function was not affected and there were no signs of involvement of the vestibular nuclei or of the intracranea! portion of the vestibular nerve (presence of a positional nystagmus). Although he was at first inclined to doubt the relation of the vestib-

ular syndrome to the epidemic parotitis, the author concluded that the viral infection was in fact the cause of it. He points to the prolonged period of incubation which according to some authors may be anywhere from 20 to 32 or even 42 days. The author found only one case previously reported in the literature of a cochleovestibular syndrome followed by parotitis. In most cases the damage was limited to the cochlear nerve. In cases where there were vestibular symptoms the lesion was in the vestibular nuclei. Many theories attempt to explain the pathogenesis; damage to the VIII nerve is the most prevalent opinion. Some authors believe that there are chemicophysical changes in the endolymph of the cochlear and vestibular apparatus. The author believes that in his case the absence of bulbar or encephalic symptoms and the isolated vestibular lesion with positional nystagmus argue in favor of a peripheral vestibular pathology in cochleovestibular complications of parotitis.

DEGASPARI

A Test of Binaural Fusion in Central Hearing Impairment

Matzker, J.: Zwanglose Abhandlungen aus dem Gebiet der Hals-Nasen-Ohren-Heilkunde, Thieme, Stuttgart, Nr. 1; pp. 117, 46 fig., 1958.

The German Z. Laryng. has recently issued Nr 1 of a series of "zwanglose Abhandlungen," i.e., articles which for reason of their length cannot be published in regular issues of the journal. With this step the Z. Laryng. has followed the example of the Acta Otolaryng .(Stockh.) which has published its supplements since 1920. (The same as the Beihefte of older German journals)

The first issue now on hand is devoted to a new clinical hearing test which is designed to evaluate central auditory impairments. The test is based on a binaural fusion technique. The book is divided into three sections: the first consists of an anatomical and physiological introduction, and a review of current audiometric testing techniques, including such methods for assessment of central impairment as those by Bocca, Schubert, a.o. The second portion gives a description of the author's own testing technique and discusses test results in normal hearing subjects. The third section is devoted to test results obtained in patients with various intracranial lesions.

The test method is based upon the well known phenomenon first described by H. Fletcher that normal intelligibility of speech signals can be maintained when one-half of the audible spectrum is presented

to one ear and the other half to the second one. In this case complete auditory fusion must be assumed to occur. In order to render the test more sensitive the author limited the two frequency bands drastically: 500 cps to 800 cps for one ear and 1500 cps to 2400 cps for the other one. Test words were selected in such a way that the distribution of formants was as evenly as possible in both frequency bands, diphthongs being found most suitable. ("The [phonetic] *oo* and *e*, for instance, were found unsuitable because their formants are exclusively in the low-frequency or high-frequency bands respectively.) Therefore the test words finally chosen are unintelligible for monaural presentation of one band only. However, on binaural presentation of both bands near perfect intelligibility is achieved indicating central auditory fusion. By limiting the intensity of presentation care is taken to avoid peripheral crosshearing. In case of binaural differences of the auditory threshold adjustments are made. This section is concluded by a critical evaluation of test interpretations: borderline cases, false positives, etc.

At the time of writing 750 persons had been tested and the results evaluated, including both normal subjects and patients with intracranial lesions. (Mentioned in the preface is a new total in excess of 1000 cases, probably representing a later date.) In 379 normal-hearing subjects classed in various age groups it was found that the ability of binaural fusion deteriorates in persons over 60 years old. That was to be expected. Somewhat surprising, however, was the finding of a subnormal ability for binaural fusion in a sizable percentage of children under 14 years of age.

So far 162 patients with various intracranial lesions have been evaluated: brain tumors, abscesses, and atrophies; chronic hypertension; multiple sclerosis; skull traumata; and epilepsy. In a high percentage of these cases (not necessarily uniform for the various diseases listed) the binaural fusion test was positive (i.e., number of mistakes larger than normal). This was so in spite of the fact that threshold audiograms frequently failed to reveal a significant loss. Speech audiometry cannot be compared properly since apparently only spoken and whispered voice tests were administered. Important although numerically small are the autopsy reports of two patients with positive tests obtained during their lives: in the areas of auditory central pathways indications of lesions were found only in the midbrain region. Incidentally, no positive test results were obtained in all cases of schizophrenia tested, although they were but few in number. These patients had no difficulty in performing the test. After reading Dr. Matzker's study, one has the distinct impression of an

original concept which in its first clinical applications has shown very promising results.

However, the reviewer may be permitted to voice some criticism which he hopes is constructive. The presentation could have been improved for the benefit of the critical reader by providing statistical data instead of giving relatively meaningless percentages. The author could have strengthened his case in many aspects. It is to be regretted that Dr. Matzker was apparently unable to enlist the collaboration of a competent Neuro-physiologist. (He has done obviously well in this respect with regard to his Pathologist.) The physiological introduction has obviously been made up "after the fact" and, frankly speaking, is in some aspects rather naive. The author is well advised to look into such matters as Auto-correlations (Colin Cherry, a.o.), Neural Auditory Inhibitions (R. Galambos), and Lateralization problems (L. Jeffress et al, E. E. David, et al, a.o.), to mention only a few examples. The assertion that presbycusis is an exclusive central auditory phenomenon could have been made only in complete unawareness of Stacy Guild's extensive histopathological studies which were correlated with audiometric findings.

However, these remarks should not detract from the potential value of the binaural fusion test as a clinical tool. It is definitely a matter which should be investigated by other audiologists. For the sake of the record, the fact must be mentioned that Dr. Matzker received the J. Zange Award from the German Otolaryng. Soc. (1958) in recognition of the contribution made by the present study.

TONNDORF

The Treatment of Ménière's Disease with Ultrasonic Sound

Altmann, Franz, and *Waltner, Jules G.*: Arch. Otolaryng. 69:7-12 (Jan.) 1959.

The authors review the work of Arslan in the selective destruction of the labyrinth, in cases of intractable Ménière's disease, with preservation of cochlear function. They have tried the method on six of their own patients, in four of whom the attacks of vertigo were eliminated. They thought that the failure in two cases was due to an insufficient amount of ultra-sound applied.

In this technique, the antrum is opened and the horizontal and vertical semicircular canals exposed and skeletonized. The ultra-

sound applicator was applied directly to the bony walls of the labyrinth. The authors feel that the treatment has sufficient merit to warrant further attempts at such therapy.

HILDING

Chelation of the Stapes Footplate

Sataloff, Joseph: Arch. of Otolaryngol. 69:1-6 (Jan.) 1959.

The author describes the effect of decalcifying the stapes by means of a chelating agent; edathamil disodium was used. All the bones treated by this agent became softened. The author states that he has used this process clinically for two years but does not give any details as to his results or how he applies it.

HILDING

Stapes Mobilization: Analysis of Results in 250 Operations

Campbell, Edward H.: Arch. Otolaryng. 68:663-672 (Dec.) 1958.

The author points out that in the past four years the advances in the technique of this operation have been rapid and of great importance and, with this advance, a steadily increasing percentage of good hearing results, from 30 to 40% in 1953 up to 70 to 80% in reports published in 1957 and 1958, has been obtained.

The original method of Rosen attempted mobilization of the stapes footplate by means of pressure on the incus, various maneuvers at the stapes head and manipulations of various kinds to the stapes footplate. In the evolution of the technique, it was found by many that more successful mobilization could be accomplished by manipulations of the footplate, with avoidance of crural fractures and dislocations of the incudostapedial joint.

In describing his technique, Campbell secures exposure of the incus and stapes in the usual manner. Palpation with the sharp curved pick or the blunt-ended mobilizer of Derlacki on the incus immediately overlying the stapes head is then made to determine three points: a) the degree of fixation of the stapes footplate, b) the looseness or rigidity of the incudostapedial joint, and c) the fragility or firmness

of the crura. With the blunt-ended mobilizer, pulsating pressure is then applied at the anterior end of the stapes footplate. If there is any suggestion of movement, pressure is then made on the incus. By a series of pressure applications, alternating between various parts of the footplate and the incus or stapes head, free movement of the footplate is eventually obtained in the majority of instances. The completeness of mobilization is determined by: free mobility of the footplate, both at the anterior and posterior ends; the detection of nystagmus occurring on light pressure on the incus; the patient's experiencing a rotatory or up-and-down movement; the characteristic feel of a mobilized footplate with easy movement inward and the quick rebound of a loosened footplate that still retains an intact annular ligament; testing of hearing, both with the middle ear open and after the drum and skin of the canal have been replaced.

A detailed audiogram is taken on the first or second postoperative day and the second test usually on the seventh to tenth postoperative day.

In analyzing the results in 250 mobilization cases, the author found that 11 or 4.4% reached to practically the normal line; 128 or 48% reached a level of 30 db or better. These two groups represented 52.4% of the cases and these individuals all had attained a practical hearing level. Fifteen patients or 6 per cent received an improvement of 15 db or more; 8.4% of the cases had hearing made worse by the operation.

A second attempt at mobilization on the same ear was made on 12 patients. In these cases it seemed that there was incomplete mobilization of the footplate and revision was aimed at more complete loosening of the footplate. Four revisions were very successful (+3 result), 3 additional had a +2 result. Three of the four revision failures later had fenestration operations and obtained excellent results. Fenestration was performed on 43 of the 112 mobilization failures; 79% of these were entirely successful and an additional 12% partially successful.

Complications encountered in this series were few and chiefly minor. The chief one was postoperative dizziness or sense of unbalance, occasionally more severe than that seen after a fenestration. A rather common complication was perforation of the tympanic membrane, but this usually healed spontaneously. One instance of apparent damage to the inner ear mechanism occurred and no adequate explanation was apparent because mobilization was not accomplished.

No instances of facial paralysis or primary infections of ear canal or middle ear occurred in this series.

The author summarized the reasons for unsuccessful mobilization: incomplete or partial loosening of the footplate; fractures of one or both crura; dislocation of the incustapedial joint; advanced diffuse otosclerotic stapes fixation; anomalies of conduction mechanism; adhesive formations in the middle ear.

HILDING

Idiopathic Haemotympanum

Birrell, J. F.: J. Laryng. and Otol. 72:769-784 (Oct.) 1958.

The author adds eight cases to the 20 he has found in the literature, six of which were seen in one year. He feels this is a clinical entity with similar history, physical, radiologic, operative and pathological findings. It must be distinguished from known causes of hemotympanum as angioma, fractured skull, abnormal jugular bulb, and blood dyskrasia.

All gave a history of persistent discomfort in the affected ear and loss of hearing. There was rarely a transient bloody discharge. Any relief from antibiotics, adenotonsillectomy, myringotomy, or tubal inflation was usually temporary. The characteristic blue drum, darkest in the *pars tensa*, was retracted, normal or bulging. The eustachian tubes were usually patent. Blood studies were noncontributory. Mastoid x-rays invariably showed clouding on the affected side.

Despite isolated cures following adenotonsillectomy, inflation, myringotomy and aspiration, the author joins other writers since 1949 in advocating a mastoidectomy (Schwartze) for permanent relief of all symptoms. At operation, mastoid cell destruction with a sterile black cellular content is found. Histological studies show giant cells and cholesterol spaces, and occasionally hemosiderin, a "cholesterin granuloma."

The author discusses other etiological theories, but expresses the opinion that the blue color is altered blood arising in the mastoid process, and perhaps too viscous to flow out a patent eustachian tube. Comparison with secretory catarrhal otomastoiditis is made. The

possibility of a virus causing a hemorrhagic response is suggested from the sterile cultures, the apparently increasing incidence, and the analogous hemorrhagic bullae, epistaxis and septal hematoma seen occasionally in influenza. Failure to treat the condition surgically, he feels, may lead to attic granulation tissue, perforation, migration of squamous epithelium, and cholesteatosis. There are 18 references.

TRIBLE

Surgery of Deafness Caused by Adhesive Otitis Media (La chirurgie des surdités par otites adhesives)

Maspétiol, Roger: Les annales d'oto-laryngologie 75:4-5:213, 1958.

Many cases of deafness due to adhesive otitis media may be helped by surgery. The principles of stapes mobilization or tympanoplasty may be used according to the type of case. The choice of surgery is dependent upon two factors: first, the etiological factor is considered and secondly, the type of lesion to be dealt with.

The author does not use the transtympanic approach as described by Rosen but uses the classical postauricular route.

In about one-third of the cases, fixation of the stapes is the only lesion; in the majority of cases, however, multiple lesions of the middle ear are found. These may consist of fibrous bands between the ossicles themselves or bands uniting the ossicles to the promontory or fibrous bands obstructing the round window.

A rigid sclerotic or even ossified stapedius tendon may be found. In many cases the attic should be explored and adhesions found linking the ossicles to the roof are removed.

The author fails to give the results obtained by his method.

MONTREUIL

Considerations on Cerebral and Cerebellar Abscesses of Otitic Origin (Considérations sur les abcès cerebro-cerebelleux otogenes)

Tzetzu, I., Ciobany, M., Dimitriu, A. V., and *Miclesco, S.*: Revue de laryngologie, otologie, rhinologie 79:7-8-449, 1958.

The authors review a series of 2,537 cases of mastoiditis at the Oto-Laryngological Clinic in Bucharest between the years 1952-1956. In this series of cases, there were 13 abscesses of either the cerebellum

or the cerebrum which represents a percentage of about 0.50. Seven of these were localized in the temporosphenoidal region while six were cerebellar. These cases represented complications arising from acute exacerbation of a chronic otitic infection. In most of these there was cholesteatoma or polypoid degeneration of the middle ear or osteitis. The most frequent routes of infection are through the tegmen, the labyrinth and the lateral sigmoid sinus. Emphasis is made on the importance of immediate surgical treatment wherever labyrinthine symptoms arise in a chronic otitis media. The authors state that the diagnosis of a cerebral abscess is most difficult to make and requires the very close collaboration of the neurologist, the ophthalmologist, the internist and the neurosurgeon. The onset of the infection is usually very insidious. The authors say that headache is probably one of the most constant symptoms, but is very indefinite in character. Vomiting exists only when intracranial hypertension occurs. In all cases, the general condition of the patient is deeply affected. The authors believe that periods of bradycardia followed by normal cardiac rhythm and rate is an important sign in making an early diagnosis of the abscess. Of the 13 cases, six died giving a percentage of 46%. Early surgical drainage, combined with antibiotic and supportive therapy is most important.

MONTREUIL

Head Injury and Impairment of Hearing

Tsuiki, T.: Oto-Rhino-Laryngologic Clinic, Kyoto, 51:1-6 (Sept.) 1958.

Seventy-six cases of head injuries and their relation to impairment of hearing are reported.

There was no characteristic change in hearing acuity. However, when roentgenographic evidence of fracture of the temporal bone was seen, there appeared to be impairment of hearing of varying degrees depending upon whether the fracture was on a horizontal or transverse axis of the temporal bone, or a labyrinthine concussion. In 20 patients there was a sudden dip in speech perception. Twenty-six patients were seen 2 to 3 months after the accidents. Forty-four patients recognized hearing impairment within 10 days of their accident. The most severe impairment was observed when the head was struck in the back portion.

HARA

Electronystagmography

Koike, Y., et al.: Oto-Rhino and Laryngological Clinic, Kyoto, 51:655-663 (Aug.) 1958.

The authors present their observations on the technical manipulation of E.N.G. and the artifacts associated with the polarization of electrode, voluntary and involuntary eye movement, E.M.G. of the ocular muscles or E.E.G. which frequently interfere with the exact analysis of the recorded nerves.

They discuss the method of direct registration of eye-speed in nystagmus. They calculated the eye-speed in the slow and the quick phase under various experimental studies. They believe that the eye-speed in the quick phase is not constant but variable. The quick and slow components are independent of each other, but intimately correlated. Thus the increase of eye-speed in the slow phase leads to the increase of eye-speed in the quick phase of nystagmus. The thory advanced by Dohlman and others that the quick phase is not related to the vestibular stimuli is doubtful according to this study.

HARA

NOSE

About Variations of Sulfocyanic Radical in Nasal Mucus Following Hematogenous Olfaction

Bartalena, G., and *Vagliani, F.*: Bollettino malattie orecchio naso gola 75:577-609 (Nov.-Dec.) 1957.

The authors briefly review three theories of hematogenous olfaction: 1) central stimulation; 2) peripheral stimulation by means of odorous particles which act on the olfactory nerve endings after having been eliminated by the lungs; 3) peripheral stimulation by elimination of the particles through the nasal mucous membrane and subsequent reabsorption through the olfactory region.

Previous experiments had shown the necessity for the existence of a specific biochemical reaction within the nasal mucosa in order for hematogenous olfaction to occur. Knowing the oxidation-reduction and catalytic functions associated with variations in the concentrations of the sulfocyanic radical (-SCN), the author performed 100 experiments on 60 persons to evaluate the variations of the sulfocyanic radical before and after hematogenous introduction of the pure-

olfactive substances (rose-hydrolate and mint-hydrolate). On the basis of the experimental results, it was shown that hematogenous olfaction does not occur within the central nervous system. It was concluded that these phenomena are carried out completely at a peripheral level. The authors believe that odors come to the olfactory region after having been eliminated by the nasal mucosa and by the rhinopharyngeal mucosa.

DEGASPARI

Malignant Granulomas of the Nose and Paranasal Sinuses

Mills, C. Peter: J. Laryng. and Otol. 72:849-887 (Nov.) 1958.

The author has reviewed 86 cases recorded in the literature and presented three more with extensive work-up. Of the 86, 60 are dead, 10 alive with disease, one lost to follow-up, one 8-year cure, and 14 apparently free of disease but for less than five years. The disease started in the nose in 67, and in the sinuses in 19. Fifty-five patients were males, and in both sexes most cases were between 25 and 55 years of age with the peak age in the late thirties. This pattern parallels periarteritis nodosa, but is younger than the age pattern for nasal and sinus neoplasms. Preceding paranasal sinus infection was reported in most of these patients, frequently with surgical attempts at relief. The staphylococcus was most commonly cultured; the streptococcus next. The early symptoms of nasal blockage and serosanguinous discharge, were followed by the destructive ulceration of the nose, sinus, palate, cheeks, and orbit. Late symptoms depended on the exact site and amount of destruction and superinfection. Of the 60 deaths, 29 were from cachexia, 9 pneumonia, 8 uremia, 4 septicemia, 3 hemorrhage, 2 cardiac failure, and the remainder from miscellaneous single causes. Almost all apparently successful cases were irradiated in doses ranging from 1500 roentgens on up.

The author's three cases were thoroughly studied. Multiple biopsies and sections of operative specimens were made, always showing chronic inflammatory cells, fibrosis, and collagen. Cultures in all three showed antibiotic sensitive strains of staphylococcus aureus. The sedimentation rates were persistently over 50 mm in the first hour in active phases of the disease. The author feels the high elevation of sedimentation rate helps distinguish this disease from a neoplasm, and may be used prognostically, as in one patient it rose sharply prior to appearance of a recurrence, and fell slowly under effective therapy.

At the height of the disease a reversal of A/G ratio occurred with a normal serum fibrinogen level. Electrophoretic studies showed the change to be a high gamma globulin, a change characteristic of the collagen diseases. Attempts at virus isolation by injection of bacterial free filtrates of the granuloma intramuscularly, intraperitoneally, and intracerebrally, into mice, rats, rabbits, hamsters, and ferrets, were unsuccessful. His first patient died following a severe epistaxis, the other two were apparently free of recurrence.

The author does not feel the disease is neoplastic, nor primarily inflammatory, but a hypersensitivity properly grouped with the collagen diseases, and frequently associated with periarteritis nodosa. He suggests the destructive granulations may represent waves of hypersensitivity in an antrum sensitized to staphylococcus, streptococcus, or some unidentified antigen.

The suggested treatment is adequate drainage at the time of biopsy followed by a prolonged course of the proper antibiotic, and about 2000 r irradiation. The clinical course can be followed with periodic sedimentation rates and blood protein examinations; urinalysis, blood urea nitrogen determinations, and chest x-rays should also be followed for early evidence of systemic periarteritis nodosa.

There are 61 references to the literature and 6 personal communications. The latter are follow-up's on patients reported well by others in earlier papers. There is a wealth of investigational data in this comprehensive article.

TRIBLE

LARYNX

Surgery After Radiation Therapy in Malignancies of the Larynx and Laryngopharynx

Oreggia, Juan Carlos: Anales de Oto-rino-laringologia del Uruguay, Vol. 28 (Part II), 1958.

The primary treatment in cancer of the larynx may be either surgery or radiation. When the chosen method of treatment fails the surgeon may resort to the other. In no case should surgery or radiation be incomplete. Both should be complete or radical to begin with. This paper is concerned with the surgical management of those cancers which were in every way given what is considered

"adequate radiation" in terms of time, field, voltage, filters, etc. The surgical indications arise from either obvious or suspected signs of malignancy. In the latter cases, biopsy is indicated. In the obvious cases it is best to plan the definitive surgical procedure and confirm the type of tumor with frozen sections. Narrow or wide field laryngectomy, with unilateral neck dissection when necessary is carried out. The author counsels against bilateral neck dissections because of the grave complications due to lymphatic stasis. Partial laryngectomies are contraindicated in patients previously irradiated. Surgery may have to be done in more than one stage, preferably under general anesthesia. Electrosurgery is also contraindicated.

There are four criteria for suitability to surgery in previously irradiated patients:

1. The length of time since the end of radiation therapy. As a general rule surgery performed after one or two years is disastrous. The optimum time is two to four months; in these cases healing has proceeded in practically normal fashion.

2. Condition of the skin and soft tissues of the neck. The reaction due to radiation is usually terminated in approximately 40 days. Observation of this reaction is helpful in determining suitability for surgery when failure of the radiation has been determined.

3. General health of the patient. This is of paramount importance. No surgery should be contemplated when there is any serious impairment, except for the obvious changes which are due to the lesion or the radiation.

4. Adequate pre-operative preparation of the patient and post-operative care. Attention to aseptic technique in surgery and dressings, supplemented by antibiotic protection. Particular care with the tracheal stoma and feeding tube is essential.

ALFARO

The Results of Treatment of Post-traumatic Laryngotracheal Stenosis

Nicelli, F.: Archivio Ital. Otologia Rinologia e Laringologia 69:61:79 (Feb.) 1958.

The author enumerates the most frequent types of lesions of the larynx and trachea which occur following trauma to the anterior and lateral regions of the neck; he discusses the immediate symptomatol-

ogy of these lesions, and the various methods employed in the treatment of laryngotracheal stenosis.

Dilatation through endoscopy or through the tracheal stoma is recommended in cases in which the scar forms a thin diaphragm; uncertain results are obtained in wide scar stenosis. Laryngofissure with insertion of a mould gives good results in some cases; but when the scar tissue involves the larynx and the first tracheal rings few good results are obtained.

The author describes the operations advocated by Figi and others, in which the scar tissue is removed and the bleeding surface covered by skin grafts kept in place by acrylic moulds. He points out that the stenosis can sometimes recur so that the work of the surgeon is in vain.

Four cases are presented which illustrate different surgical techniques.

DE GASPARI

PHARYNX

Abnormal Sensation in the Pharyngolaryngeal Region (Lump in the Throat)

Nunomura, T., et al.: Clin. Otolaryngol. 51:1003-1006 (Dec.) 1958.

This study is based on observations made on 48 patients having the complaint of abnormal sensation in the throat. There were 23 in whom no objective evidence of abnormality was revealed. However further systemic examination disclosed parasitic invasion of the throat in seven; anemia in nine; hormone deficiency in three; lues in one; allergy in one; and two unknown.

In the light of this investigation the authors urge the making of an objective diagnosis in each one, and the institution of appropriate treatment. Since the incidence of anemia and helminthiasis was notably high in this series, the quantitative determination of serum iron and search for parasitic eggs may be considered necessary procedures.

HARA

PHARYNX and LARYNX

Histological Studies of Tonsils in Infectious Mononucleosis

Schwarz, M.: Medizinische, Nr 45, 1803-1805, 1958.

The author removed the tonsils from eight patients with infectious mononucleosis at various intervals after the acute stage of the disease, i.e., between the sixth and twenty-first day. In two of these cases the tonsillectomy was unilateral and follow-up studies were conducted by removing the second tonsil after four to six months. All material was studied histologically.

First, the normal tonsillar anatomy is briefly described with its capsule and trabeculae, its crypts, lined with squamous epithelium, and its lymphatic stroma, which contains the lymph follicles. Each follicle is differentiated into a "light zone" and a "dark zone," the latter sitting like a cap upon the former and pointing toward the lumen of the crypt. Each follicle (light and dark zones) and the adjacent epithelium of the crypt is believed to form a functional unit. In previous papers, the author has used the term "histosystem" for these units. Two Italian authors, Fioretti and Pirro, have described them as "cryptolymphons" and "adenons" respectively.

With respect to infectious mononucleosis, the author differentiates three stages on the basis of histological findings. First, (Acute) Stage: Exudative inflammation within the crypts penetrating into the lymphatic stroma and leading to epithelial necrotization and formation of pseudo-membranes. The lymphatic stroma becomes undifferentiated (homogenization). Even the tissue of the trabeculae and of the capsule becomes edematous.

Second, (Reactive) Stage: Around the ninth day, the epithelium, in places where it had not become necrotic, becomes hyperplastic, first in an irregular manner, later more regularly, that is, forming a zone of basal cells. At the same time the sloughing-off of the necrotic material is still going on. The lymphatic tissue remains undifferentiated (homogenized) and contains numerous plasma cells and lymphocytes. The capillaries increase in number.

Third, (Regenerative) Stage: Formation of groups of large plasma cells. These groups take on the appearance of the "light zones" of normal follicles. They are surrounded by a wall of lymphocytes. Active mitosis is seen. The new light zones expand toward the lumen of the crypts, while the lymphocytic walls regroup so as to

form the cap-like "dark zones." At the same time, the epithelium is completely regenerated and gradually attains its normal thickness. Oftentimes, the redifferentiation of the lymphatic stroma is not complete. Homogeneous lymphatic tissue persists in some areas. The entire process of regeneration takes from three to six months.

TONNDORF

A New Technique for Radiographic Visualization of the Laryngeal Ventricles with Lipiodol

Galioto, G. B., Ruju, P.: Bollettino delle Malattie Dell'Orecchio, Della Gola, Del Naso 75:675 (Nov.-Dec.) 1957.

The authors describe a new technique for better radiographic visualization of the laryngeal ventricles.

A Magill tube is introduced into the trachea; the space between the tube and the tracheal wall is filled with lipiodol. After the radiograms are taken the lipiodol is removed by suction through a small tube.

This technique has yielded good results in the visualization of lesions which were poorly seen by means of endoscopy and the usual x-ray procedures.

DE GASPARI

MISCELLANEOUS

Submaxillary Salivary Flow: A Test of Chorda Tympani Nerve Function as an Aid in Diagnosis and Prognosis of Facial Nerve Paralysis

Magielski, John E., and *Blatt, Irving M.*: Laryngoscope 68:1770-1789 (Oct.) 1958.

The authors describe what they consider a more accurate test of motor function of the chorda tympani nerve. Polyethylene catheters are inserted into each Wharton's duct; the patient sucks on a slice of lemon for 60 seconds during which time the salivary output from each submaxillary gland is measured.

Normal control subjects between the ages of 10 and 60 years were shown to produce approximately equal amounts of secretion. Four categories demonstrating malfunction of the chorda tympani

are presented. Data is included on the following: 1) two cases of chronic otitis media and mastoiditis; 2) four patients with Bell's palsy; 3) three cases of facial nerve paralysis associated with skull fractures and 4) one case of facial nerve paralysis associated with central nervous system disease.

On the basis of these observations, it is believed that this procedure is a more accurate measure of chorda tympani function than tests for taste. The authors suggest that the evidence points to a good prognosis for spontaneous recovery of facial nerve function if chorda tympani function is retained or is regained early.

SENTURIA

Stuttering

Otsuki, H.: Clinical Otolaryngology, Kyoto, 51:1150-1186 (Dec.) 1958.

The study is based on 331 patients. About one-half of these 331 were under ten years of age. The proportion of male to female is 11:1. The majority of these find it difficult to pronounce vowels. Of these 331, 41.7 per cent showed a hereditary influence. The stuttering is classified as 1) repetition, 2) prolongation, and 3) blocking. Most of the stutterers tend to be sympathicotonic on phonation. Chlorpromazine is a useful drug in the control of nervous tension.

HARA

Mixed Tumors of the Parotid Gland. Postoperative Course and Histological Aspects

Pennetta, G.: Bollettino malattie orecchio naso gola 75:644-663 (Nov.-Dec.) 1957.

The author reviesw the accepted point of view regarding the biological behavior of these tumors as well as the various morphological classifications. The histological examination can give information about the structure of the tumor and can reveal signs of malignancy, but it cannot give any information about the future course of the disease. The author describes the hystological findings of 60 cases of mixed tumors operated upon during the past ten years. He states that the findings of these slides are those usual for mixed tumors. Pearl formations and groups of spinous cells of the epidermoid type containing cellular protoplasm are rare findings. No valid conclusions

can be offered which will contribute to solve the problem of the genesis of mixed tumors. The genetic hypotheses of several authors are discussed. The subjective symptomatology in all cases has been very mild, even in cases of mixed tumors of the soft palate; there is usually no difficulty in chewing, phonation or salivary secretion. Forty-eight per cent of these tumors were first noticed between the ages of 41 and 60. From the histological picture it is not possible to predict the likelihood of recurrences. Malignant changes were seen in 17 per cent of the patients. The author concludes that considering the modern surgical approaches and because of the high percentage of recurrences it is advisable to treat these tumors with radical surgery.

DEGASPARI

Books Received

Nordisk Laerebog I Oto-Rhino-Laryngologi (Scandinavian Textbook of Oto-Rhino-Laryngology)

Edited by: *Nylén, C. O., Andersen, H. C., Leegaard, Truls, and Siirala, Urpo.* 482 pp., 275 figures and 5 color-plates. Copenhagen, Ejnar Munksgaard Ltd., Price: Dan. Cr. 78.00.

Streptomycin and Dihydrostreptomycin

By *Louis Weinstein, Ph.D., M.D.*, Professor of Medicine, Tufts University School of Medicine; Lecturer on Infectious Disease, Harvard Medical School; Chief of the Infectious Disease Service and Senior Physician, Medical Service, New England Center Hospital, Boston, Massachusetts; and *N. Joel Ehrenkranz, M.D.*, Assistant Professor of Medicine, University of Miami School of Medicine; Chief of the Infectious Diseases Section, Jackson Memorial Hospital, Miami, Florida. Pp. xi & 116, 13 figures and 7 tables. Under editorial direcation of *Henry Welch, Ph.D.* and *Felix Marti-Ibanez, M.D.* Antibiotics Monographs / 10, New York, Medical Encyclopedia, Inc., 1958. (Price $4.00)

This is a very clear, concise and up-to-date review of the available information regarding streptomycin and dihydrostreptomycin. The material is presented in a brief but informative manner while, for those who desire further data, a very complete bibliography is included.

This monograph will be of particular value to those otolaryngologists who are interested in the action of these drugs upon Gram-negative bacilli found in the ear and upper respiratory tract and to those who are concerned about the untoward reactions observed in the cochlea and vestibule.

Notices

AMERICAN LARYNGOLOGICAL ASSOCIATION

Copies of the Transactions of the American Laryngological Association are available for general distribution at $8.00 a copy. Please send request with check to Dr. James H. Maxwell, Editor, Transactions, Out-Patient Bldg., University Hospital, Ann Arbor, Mich.

AMERICAN ASSOCIATION FOR CLEFT PALATE REHABILITATION

The American Association for Cleft Palate Rehabilitation will hold its 17th Annual Convention at the Sheraton Hotel in Philadelphia on Thursday, Friday and Saturday, April 30, May 1 and 2, 1959.

This Association is composed of medical, dental and paramedical specialists interested in the subject.

INTERNATIONAL CONFERENCE ON COMMUNICATIONS AND LANGUAGES

Organized by the Department of Otolaryngology of the Faculty of Medicine of Paris, the French Society of Phoniatry, the Department of Neurophysiology of the College of France, the Acoustical Physiology Laboratory, the Research Study Centre of Aviation Medicine and the Compagnie Francaise d'Audiologie, a Conference on Communications and Languages was held on January 22-25 at the new Faculty of Medicine in Paris, under the presidency of Professor Maurice Aubry. Professor Aubry is the head of the Department of Otolaryngology,

and the President of the forthcoming Seventh International Congress of Otolaryngology which will take place in Paris in 1961.

Some of the subjects discussed were the Physical, Mathematical and Philosophical Aspects of Language, Physiology of Language, Animal Signals and Human Languages, the Statistics of Vocabulary, Intelligibility and kindred matters.

THE INTERNATIONAL ASSOCIATION OF LOGOPEDICS & PHONIATRICS

It has been announced that those unable to attend the Congress, but who would like to secure a copy of the Report of the Proceedings, can obtain it at the reduced rate of seventeen shillings and sixpence (17/6d.) by ordering in advance, enclosing payment, from the Secretary before August, 1959. Secretary's address: Peggy Carter, L.C.S.T., 46, Canonbury Square, London, N.1.

PAN-PACIFIC SURGICAL ASSOCIATION

The Eighth Congress of the Pan-Pacific Surgical Association will be held in Honolulu, Hawaii, September 28 through October 5 in 1960.

All members of the profession are cordially invited to attend and are urged to make arrangements as soon as possible if they wish to be assured of adequate facilities.

An outstanding scientific program by leading surgeons promises to be of interest to all doctors. Nine surgical specialty sections are held simultaneously.

Further information and brochures may be obtained by writing to Dr. F. J. Pinkerton, Director General of the Pan-Pacific Surgical Association, Suite 230, Alexander Young Building, Honolulu 13, Hawaii.

UNIVERSITY OF BORDEAUX

A practical course of surgical techniques in otological functional micro-surgery, conducted by Michel Portmann, will be given from July 1st to July 10th, 1959, in English.

During this period every assistant attending the course will be enabled to watch surgical interventions in the theatre, to follow theoretical courses illustrated with films regarding the major techniques, and to work on his own daily anatomical specimen with all the requisite material, including the binocular microscope.

Fees: 100 francs (to be paid at the Faculty of Medicine in Bordeaux at the beginning of the course).

Applications should be sent to Dr. Michel Portmann, 45 Cours Foch, Bordeaux, France.

GERMAN SOCIETY MEETS

The German Society for Nose and Throat doctors will meet in Bad Godesberg, May 10-14, 1959, under the chairmanship of Dr. F. Zöllner, Freiburg. The theme will be Nasopharyngeal Tumors, and Functional and Psychogenic Diseases of the Nose, Throat and Ear.

Prof. Meyer zum Gottesberge, Secretary

AERO MEDICAL ASSOCIATION

The 30th Annual Meeting of the Aero Medical Association will be held at the Statler Hotel, Los Angeles, California, April 27-29, 1959. Charles I. Barron, M.D., Lockheed Aircraft Corporation, will be the General Chairman.

AMERICAL MEDICAL ASSOCIATION

Section on Laryngology, Otology and Rhinology

108th Annual Meeting, Atlantic City, June 8-12, 1959

PROGRAM

(Each paper, except those of the Guest of Honor and Chairman, will be followed by an open discussion period; questions and comments from the floor are encouraged.)

Tuesday, June 9 - 2 p.m.

Prof. Dr. H. H. Naumann, Würzburg, Germany

Intravital Observations of the Nasal Mucous Membrane (Film)

George M. Coates, M.D., Philadelphia, Pa.

Address of Guest of Honor

Gordon D. Hoople, M.D., Syracuse, N.Y.

Modern Otolaryngology

F. W. Davison, M.D., Danville, Pa.

Laryngeal Obstruction in Children

Ben T. Withers, M.D., Houston, Texas

Facility in T&A Management: Conclusions from 2400 Consecutive Cases

Joseph H. Ogura, M.D., St. Louis, Mo.

Cancer of the Pharynx, Larynx and Upper Esophagus; Surgical Aspects

Business Meeting:

Report of Section Delegate to AMA House of Delegates—

Gordon F. Harkness, M.D., Davenport, Iowa
Dean M. Lierle, M.D., Iowa City, Iowa, Alternate

Report of Section Representatives to Board of Governors of American College of Surgeons—

Roderick Macdonald, M.D., Rock Hill, S.C.
Edley H. Jones, M.D., Vicksburg, Miss.
John J. Conley, M.D., New York, N.Y.

Report of Nominating Committee—

F. W. Davison, M.D., Danville, Pa.
Louis E. Silcox, M.D., Philadelphia, Pa.
John D. Singleton, M.D., Dallas, Texas

WEDNESDAY, JUNE 10 - 2 P.M.

J. W. Hampsey, M.D., Pittsburgh, Pa.

Current Concepts of Etiology and Management in Otolaryngic Allergy

Victor R. Alfaro, M.D., Washington, D.C.

Address of Section Chairman

Henry S. Kaplan, M.D., San Francisco, Calif.

New Horizons in the Radiotherapy of Malignant Diseases

John A. Kirchner, New Haven, Conn.

Facial Bone Injuries

M. R. Himalstein, M.D., Bay Pines, Fla.

Obliterative Frontal Sinus Surgery Using Gelfoam

J. M. David, M.D., New York, N.Y.

Malignant Melanoma of the Nose and Paranasal Sinuses, and Juvenile Melanoma of the Nose

WEDNESDAY EVENING, JUNE 10 - 6:30 P.M.

Social Hour and Dinner Honoring the Guest of Honor of the Section, Dr. George M. Coates

THURSDAY, JUNE 11 - 2 P.M.

Joseph L. Goldman, M.D. and Harry Rosenwasser, M.D., New York, N.Y.

Current Concepts of the Management of Otitic Infections

Merle Lawrence, Ph.D., Ann Arbor, Mich.

Ear Physiology

Edward W. Harris, M.D., Columbus, Ohio

Symptoms Referable to the Eustachian Tube

George Kelemen, M.D., Boston, Mass.

Maternal Diabetes and Congenital Deafness

Joseph Sataloff, M.D., Philadelphia, Pa.

Stapes Mobilization with Long-Standing Otosclerosis

Howard P. House, M.D., Los Angeles, Calif.

Polyethylene in Middle Ear Surgery

THE GOULD AWARD

The International Committee for the Gould Award announces the selection of the recipient for the year 1958: Professor Fumio Nakamura, M.D., Kyoto Prefectural Medical College, Kyoto, Japan, for his electrophysiological studies of laryngeal function.

The International Committee for the Gould Award for 1959 will consist of Sir Victor Negus, 149 Harley St., London, W. 7; Professor Cotoji Satta, No. 111 Morikawa-cho, Bunkyo-ku, Tokyo; and Hans von Leden, M.D., Medical Director, The William and Harriet Gould Foundation, 30 Norch Michigan Avenue, Chicago 2, Illinois. The amount of the Award has been increased to $300.00.

MOUNT SINAI HOSPITAL

An intensive Course in Rhinoplasty, Reconstructive Surgery of the Nasal Septum and Otoplasty will be given July 11, 1959 to July 24, 1959 by Dr. Irving B. Goldman and staff at Mount Sinai Hospital in affiliation with Columbia University.

Candidates for the Course should apply to the Registrar for Postgraduate Medical Instruction, The Mount Sinai Hospital, 5th Avenue and 100th Street, New York 29, New York.

AMERICAN SOCIETY OF FACIAL PLASTIC SURGERY

The next meeting of the American Society of Facial Plastic Surgery will take place on July 15, 1959, in New York.

NEW YORK EYE AND EAR INFIRMARY

The Annual Spring Meeting of the Alumni Association of the New York Eye and Ear Infirmary will take place April 20-22, 1959, at the Infirmary.

Symposia will be offered on Headache; Allergy and Immunology in Otolaryngology; Diagnosis and Treatment of Laryngeal Conditions; Hearing Rehabilitation; and Rhinoplasty. In addition, there will be a closed circuit television demonstration of Head and Neck Surgery.

Additional information may be obtained by writing to Dr. John R. Finlay, Secretary, Alumni Association, 218 Second Avenue, New York 3, N.Y.

PACIFIC COAST
OTO-OPHTHALMOLOGICAL SOCIETY

The annual meeting of the Pacific Coast Oto-Ophthalmological Society is to be held May 3-7, 1959, at the Hotel Riveria, Las Vegas, Nevada. Guests speakers will include: R. R. Newell, M.D., William P. Mikkelsen, M.D., James F. Crow, Ph.D., Stuart C. Cullen, M.D., George E. Shambaugh, Jr., M.D., Sidney Riegelman, Ph.D., Lawrence R. Boies, M.D., Dean M. Lierle, M.D., A. Edward Maumenee, M.D., John W. Henderson, M.D., and Digby Leigh, M.D.

For details please communicate with Homer E. Smith, M.D., 686 Twelfth Avenue, Salt Lake City 3, Utah.

ANNALS

The ANNALS wishes to repurchase copies of the March 1955 and the March 1957 issues, which are out of print, at two dollars a copy. These should be delivered to Manager of the ANNALS, P. O. Box 1345, Central Station, St. Louis 88, Mo.

OFFICERS

OF THE

NATIONAL AND INTERNATIONAL

OTOLARYNGOLOGICAL SOCIETIES

American Academy of Ophthalmology and Otolaryngology

President: Dr. LeRoy A. Schall, Boston
Executive Secretary: Dr. William L. Benedict, Mayo Clinic, Rochester, Minn.

American Board of Otolaryngology

President: Dr. Gordon D. Hoople, Syracuse, N.Y.
Secretary: Dr. Dean M. Lierle, University Hospital, Iowa City, Iowa

American Broncho-Esophagological Association

President: Francis W. Davison, M.D., Danville, Pennsylvania
Secretary: F. Johnson Putney, M.D., 1712 Locust Street, Philadelphia 3, Pa.
Meeting: The Homestead, Hot Springs, Va., March 10 and 11, 1959

American Laryngological Association

President: Fred W. Dixon, M.D., Cleveland, Ohio
Secretary: James H. Maxwell, M.D., Ann Arbor, Mich.
Meeting: The Homestead, Hot Springs, Va., March 8 and 9, 1959

American Laryngological, Rhinological and Otological Society, Inc.

President: Dr. Gordon D. Hoople, Syracuse, N.Y.
Secretary: Dr. C. Stewart Nash, 708 Medical Arts Bldg., Rochester, N.Y.
Meeting: The Homestead, Hot Springs, Va., March 10, 11, 12, 1959

American Medical Association, Section on Laryngology, Otology and Rhinology

Chairman: Victor R. Alfaro, M.D., Washington, D.C.
Secretary: Walter E. Heck, M.D., San Francisco, Calif.
Meeting: Atlantic City, June 8-12, 1959

American Otological Society

President: Moses M. Lurie, M.D., Boston, Mass.

Secretary-Treasurer: Lawrence R. Boies, M.D., University of Minnesota Hospitals, Minneapolis 14, Minnesota

Meeting: The Homestead, Hot Springs, Va., March 13 and 14, 1959

The American Society of Ophthalmologic and Otolaryngologic Allergy

President: Joseph W. Hampsey, M.D., Grant Bldg., Pittsburgh 19, Pa.

Secretary-Treasurer: Daniel S. DeStio, M.D., 121 S. Highland Ave., Pittsburgh 6, Pa.

Pacific Coast Oto-Ophthalmological Society

President: H. Leroy Goss, M.D., 620 Cobb Building, Seattle 1, Wash.

Secretary-Treasurer: Homer E. Smith, M.D., 508 East South Temple, Salt Lake City, Utah

The Society of Military Otolaryngologists

President: Lt. Colonel Stanley H. Bear, USAF (MC)

Secretary-Treasurer: Captain Maurice Schiff, MC, USN, U. S. Naval Hospital, Oakland, California

Canadian Otolaryngological Society

President: Dr. G. Arnold Henry, 170 St. George St., Toronto, Ontario

Secretary: Dr. Donald M. MacRae, 324 Spring Garden Road, Halifax, Nova Scotia

Meeting: Sheraton-Brock Hotel, Niagara Falls, Ontario, October 9 and 10, 1959

Mexican Society of Otolaryngology

President: Dr. Rafael Giorgana

Secretary: Dr. Carlos Valenzuela, Monterrey 47 Mexico 7, D.F.

Pan-American Association of Oto-Rhino-Laryngology and Broncho-Esophagology

President: Dr. Jose Gros, Havana

Secretary: Dr. Chevalier L. Jackson, 3401 N. Broad St., Philadelphia 40, Pa.

International Bronchoesophagological Society

President: Dr. Jo Ono, Tokyo

Secretary: Dr. Chevalier L. Jackson, 3401 N. Broad St., Philadelphia 40, Pa.